Transitioning the Pediatric Urology Patient
The Abnormal Pediatric Bladder: Is the Time Bomb Ticking?

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Transition: Part of Ageing Process
Transitioning

“The purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-oriented health-care systems.”

Blum RW. J Adolesc Health 1993
Transition from child-centered to adult health-care systems for adolescents with chronic conditions

Transition ≠ Transfer
Transitioning

“Process by which adolescents and young adults with chronic disease are prepared to take charge of their lives. It is an educational process that ideally begins before children reach adolescence and continues until they are capable of taking full responsibility of their care.”

Knauth A. Cardiol Clin 2006
Transition and transfer from pediatric to adult care of the young adult with complex congenital heart disease

Transitioning Process

- Increases likelihood of continuity of care
- Increases patient compliance
- Improves self advocacy

A Natural History Study of Adolescents and Young Adults with Sickle Cell Disease as They Transfer to Adult Care: A Need for Case Management Services.
Urological Examples

- Spina bifida
  - In the 1970’s less than 1/3 survived beyond age 20
  - Today, greater than 80% do

- Bladder extrophy
  - Improved bladder function
  - Psychosexual issues

Transitioning:
Fundamental Elements

- Professional and institutional support for transition of care
- Family support
- Encouragement of change in decision-making and consent from parents to adolescent
### Transitioning: Fundamental Elements

- Professional sensitivity to psychosocial aspects of disability
- Primary, preventive medical care for chronic illness
- Health education: patient, family & transitional providers

### Transitioning: Major Barriers

- Upper age limits – pediatric hospitals *(anesthesia driven in most children’s hospitals: 18-21)*
- Insurance coverage & reimbursement
- Availability & interest of specialty care
- Practice differences – adult vs. pediatric
  - Organization of care
  - Communication
  - Family involvement
How are we doing in the U.S.?

Transition of care

- From the “Children’s Hospital” perspective:
  - Inconsistent process across specialties
    (and within departments!)
  - Referrals – erratic, not systematized
    toward physicians, hospitals
  - Paucity of expert psychological support
  - Institutional barriers to “integrated care”

- From “General Hospital” perspective:
  - More difficult to accomplish transition?
    - Reduced accessibility of adult specialist(s); lack of program based models
    - Unfamiliar facility/system with less “hand holding”

No evidence yet!!!
Financing:
Health Insurance in the U.S.

- Adult:
  - Employer based or individually purchased
  - Medicare, Medicaid

- Barriers include:
  - Employability
  - Pre-existing condition

Financing:
Health Insurance in the U.S.

- Parental coverage
  - Variable limits (19-25); employer dependant
  - Extended coverage to adulthood (dependant on disability status)

- Medicare: safety net for disabled
  - Not limited by parental income
  - At 19, continuing benefits based on adult disability guidelines
    - Coverage less broad than for child
Model System

- Not yet established
- No evidential basis for what works
- Health care is a moving target

Current Efforts

- Establish hospital-hospital based transition program that incorporates all departments
- Involve social work, psychiatry, “liaisons” between practitioners/hospitals
- Ongoing research to develop evidence based data on which to model the transition process

Who will foot the bill?
The Abnormal Pediatric Bladder

This is a problem! A big problem!
Is it getting bigger?

[Images of CT scan and histology]
Metastatic Adenocarcinoma After Augmentation Gastrocystoplasty

- 2/72 pts with GC
- Mean age augment- 5.5 years
- Mean age dx- 19.5 years = 14 yr. mean lag time to dx
- NO hematuria!
- NO recurrent UTI!
- NO pain!
- NO lesions on cystoscopy!

Pt 1
- L2-3 MMC
- GC + Mitrof (Appendix)/AUS
- ANNUAL cysto- neg
- Presented with liver/LN mets
- Liver bx (+) adenocarcinoma
- Urine cytology (+)

Pt 2
- PUV
- GC & Mitrof (Appendix)
- LRD x 7 yrs wuth ANNUAL (-) RUS
- Presents with increasing hydro
- Cysto/cyt –metaplasia only
- CT-mets- Ex lap- - - (+) adenocarcinoma


Objectives

- Presentation and pathology of bladder cancer in the patient with an “abnormal pediatric bladder”
- Treatment and outcome bladder cancer in “former” pediatric patients with bladder abnormalities
- Learn the pros/cons of screening this population for bladder cancer
- Understand that bladder augmentation is only 1 potential risk factor and not necessary for the development of bladder cancer; CIC may be worse!
Historical Background

Increased incidence of tumors in USO
- 8 fold increase risk of colon cancer - 6th decade of life
- Adenocarcinoma at ureteral enteric anastomosis
- Hypothesized this was due to the fecal urinary mixture
- Bladder augmentations free from the mixture of feces and urine would be free from malignant transformation

- Gittes 1986, Husmann & Spence 1990

Hypothesis: Questions

• A increased risk of malignancy following bladder augmentation for TB and shistosomal cystitis
  - TB and shistosomal infections, i.e. “damaged, inflamed bladder” – predispose to cancer

• Hypothesis: increased risk of cancer following augmentation for congenital bladder abnormalities???????

- Filmer & Spencer 1990
Risk Factors

- Urinary stasis
- Ph changes
- Nitrosamines
- Infection
- Calculi
- Foreign body
- Anastamotic line!!!

Many, theoretically reduced with gastrocytoplasty

Cancer in Congenital Bladder Dysfunction

- Increased risk of adenocarcinoma of the bladder in extrophy +/- augmentation
- Neurogenic bladder- spina bifida
  - Histologically abnormal
  - Increased risk of malignancy in NGB-controversial

Conundrum

• Is bladder augmentation an independent risk factor for cancer?

• Is there an inherent risk of malignancy in the dysfunctional bladders we are augmenting?

Reports of Cancer Following Augmentation for Congenital Anomalies

• Enteric cystoplasty
  – 13 cases and 1 adenomatous polyp
    Ileal augments 9 cancers
    Colon augments 3 cancers and 1 polyp

• Gastric cystoplasty
  – 9 cases

MMC and Bladder Ca

  - 3 pts. (Age 44, 37, and 29). Cecal and Ileocecal Augmentation
  - All Died
  - Recommended yearly cysto and screening for bladder Ca
    - 10 years after bladder augmentation
  - 3 patients (Age 32, 24, & 34) Gastric
  - All alive at mean f/u 23 mo.
  - Recommended yearly cysto and screening for bladder Ca.
    - Annual U/S, cystoscopy 10 years after gastrocystoplasty

MMC and Bladder Ca: U of Iowa Series

- 1995-2006
  - 10 patients (8 female, 2 male)
- Median Age 37 years (range 20-60)
- Presentation
  - Gross hematuria
  - Difficulty cathing/ changing cath
  - UTIs/ Urosepsis
  - Sterile Pyuria

MMC and Bladder Ca: Univ. of Iowa Series

- Pathology
  - TCCa – 60%
  - AdenoCa – 20%
  - Squamous Cell Ca – 20%
- Stage
  - T2 - 10%
  - T3/4 - 90%
  - Nodes (+) - 40%

- Treatment
  - Radical Cystectomy - 80%
  - Radiotherapy - 20%
  - Died at presentation (age 20-F)
  - Sigmoidectomy - 10%
  - Chemotherapy - 30%

- Median Survival – 15 months
- Only 1 patient had T2N0 disease and is alive and disease free at 20 months
- 1 patient is alive with liver metastases at 8 months
- 6/10 patients had regular, yearly visits with a urologist
  - UA, Labs, Ultrasound
- Only 2/10 (20%) had bladder augmentation (8, 14 yrs) but all were on CIC

MMC and Bladder Ca: Univ. of Iowa Series

- Median: 15 mo
- Mean: 22 mo

Advanced Stage at Diagnosis - High Mortality

- T3-T4 or widely metastatic disease
  - 54% (12/22)
- Dead of disease
  - 81% (18/22)

Current Recommendations for Surveillance following Bladder Augmentation

Assumed increase incidence cancer

Advanced stage at Dx

- 5-10 yrs post augment- Annual F/U
- Cytology
- Cystoscopy
- Radiographic studies

- Filmer and Spencer 1990, Lane & Shah 2000, Soergel et al 2004

Mayo Clinic:
Enterocystoplasty- Prospective Data Base

- All patients seen since 1986: n=385
- Faults
  - 45% (173/385) had their augment elsewhere
    - Referral bias?
  - 153 pts followed > 10 yrs post augment
    - F/U: some pt >50 yrs post augment
    - 16% (25/153) ileal conduits to undiversion
    - Time started: ileal conduit formed not augment
Incidence of Bladder Tumors Following Enteric Augmentation (patient population)

Followed 153 patients
- 109 ileal augments & 44 colon augments
- Minimum of 10 yrs post augment
- No patient with a Hx: fecal urinary slurry
- Etiology
  - Neurogenic 97 pts
  - Exstrophy-epispadias 38 pts
  - PUV 18 pts

Incidence of Bladder Tumors Following Enteric Augmentation

- Median F/U 27 yrs (Range 10-53 Yrs)
- 4.5% (7/153 pts) developed a malignancy
  - Median time to tumor; 32 yrs, range 22-52
  - Median age tumor Dx; 52 yrs, range 30-61
  - 1.5% per decade post augment

- Husmann & Rathbun J Ped Urol 2008
Enteric Augments for: Neurogenic Bladder (N=97 pts)

NGB- Cases of malignancy
- 2% (2/97 pts)
- TCC
  - tobacco usage ≥ 2PPD for > 25 yrs
- Wide spread bladder mucosal involvement
- Cystectomy and ileal conduit – 2 pts
  NED at 5 & 6 yrs post op

Enteric Augments for: Exstrophy Complex (N=38 pts)

Cases of Malignancy – Exstrophy
- 8% (3/39 pts)
- Predominantly adenocarcinoma (mixed)
- Wide spread bladder-aug involvement -3 pts
- Metastatic at Dx– 1 pt
- Cystectomy and ileal conduit -2 pts
  DOD at 1-3 yrs – 3 pts
Enteric Augments for:
Posterior Urethral Valves (N=17 pts)

PUV- Cases of Malignancy
- 12% (2/17 pts)
  - Both pts with CA with Renal Tx & viral cystitis
    22 and 25 years post transplant
  - Poorly differentiated tumors (mixed cells)
  - Tumors wide spread arising in augment
  - Cystectomy, stopped immunosuppressives

  DOD 2 yrs post op – 2 pts

Cancer in Enteric Bladder Augmentations

- Risk of malignancy post enteric augment:
  - 1.5% per decade

- Advanced stage at Dx:
  - >70% T3-4 N1

- High Risk Patients
  - tobacco exposure
  - immunosuppressants & viral cystitis
  - exstrophy
Reality: We are not augmenting a normal population!

Population are all on CIC – chronic bacteriuria & repeated trauma of catheterization

- Neuropathic bladders
- PUV on immunosuppressives
- Exstrophy patients

Cancer Incidence
Augment vs Dysfunctional bladders

- N= 153 pts with augments
- N = 589 pts with dysfunctional bladders followed
- Age (+/- 2 yrs)
  - Median 41 yrs (range 17-65)
- Etiology of bladder dysfunction- matched
  - Neurogenic (63%), Exstrophy (25%) PUV (12%)
Unknown differences between two study population

Unknown differences in:
- tobacco usage
- family history of bladder cancer
- industrial exposure

Incidence of Cancer

- Augmentation & CIC
  - 4.5% (7/153pts)
  - Median time to tumor 32 yrs, range 22-52
  - Age at tumor Dx, median 52 yrs, range 30-61

- Bladder dysfunction & CIC
  - 2.6% (4/153)
  - Age at tumor Dx, median 50 yrs, range 38-62
Incidence of Malignancy Following Enterocystoplasty vs Matched Controls

- Augmented population (Enteric)  - 4.5% (7/153)  6-7 fold increase*
- Etiology controlled population with CIC alone  - 2.6% (4/153)  3-4 fold increase*
- Normal population**  - 0.7%  *Not statistically different  ** p <0.05

*Not statistically different  ** p <0.05
### Hypothesis for Cancer Following Bladder Augmentation

**Multiple stimuli (multiple hit inducer)**
- Primary abnormality of the bladder (exstrophy, neurogenic bladder?)
- Augmentation
- CIC, bacteriuria
- External stimuli (tobacco, immunosuppressives)

### Tissue Engineered Bladders-
Will the future bring a panacea???
Hypothesis and concerns with tissue engineering in dysfunctional bladders

Tissue Engineering
- Abnormal native bladder cells - harvested
- Raised in vitro and placed on scapholds
- Under the influence of growth factors
- Replaced back in hostile environment
- Impact on mutagenesis - unknown

Current Recommendations for Surveillance

Assumed increase incidence cancer
Advanced stage at Dx
- 5-10 yrs post augment- Annual F/U
- Cytology
- Cystoscopy
- Radiographic studies

Seek & Ye Shall Find…… Maybe Not!

Is Screening Going to Help?

- Low incidence
  - Bowel augmentation 4.2%
  - Gastrocystoplasty 10%
- Gastrocystoplasty- 2/4 patients had cysto within 1 year of dx
- Iowa MMC patients- 6/10 followed yrly by urologist
- Is more than an annual visit going to be necessary?
Spinal Cord Injury and Bladder Ca

- Increased risk of bladder Ca
- Mean time from injury to Ca 23-34 years
  - 20 years TCCa
  - 32 years SCCa
- Risk factors
  - Indwelling Cath > 8 yrs
  - Bladder stones

Screening Studies in SCI
- Most studies don't show significant benefit
  - Lower stage
  - Better survival
- Not cost effective!!!

Surveillance of Augments (50 pts 5 yrs)

- 40 ileal and 10 colonic augments
- Median time from augment when placed on study was 18 yrs range 10-30
- Median age at initiation 28 yrs (24-40)
- Not selective
  - 43 NGB, 5 PUV (3 with Tx), 2 Exstrophy

- Higuchi & Husmann AUA 2009
Surveillance of Augments
(50 pts 5 yrs)

• Urine cytology positive in 26/250 (10%)
  – No bladder malignancy
  – Specificity 90%; sensitivity unknown

• Endoscopy found 1 suspicious lesion
  – Biopsy revealed adenomatous polyp
  – Colon augment & immunosuppressed pt

Annual
Cytology & Endoscopy

• Tumor incidence: 1.5% per decade

• Cytology:
  – Specificity poor: Sensitivity unknown
  – Costly test ($460) with little proven benefit in this pt population

• Endoscopy
  – >950 to Dx one malignancy
  – Cost ($625)
Annual Cytology & Endoscopy

Estimated cost
>$950K
to Dx 1 cancer

Are there clues that indicate the need for endoscopy? (7 malignancies & 1 polyp)

- Radiographic abnormalities - 6/8 (75%)
- Gross hematuria - 5/8 (62%)
- >4 Sx UTI in one yr; - 4/8 (50%)
- Pelvic/Bladder pain - 3/8 (38%)
- 7/8 (87%) had one or more of the above indications for endoscopy
- 1 asymptomatic pt (Renal Tx)
Decision Points 
(Annual Visits: Lytes, Creat, B12 & UA)

• If history – positive
  – > 4 symptomatic UTI in a year
  – Chronic pelvic, perineal flank pain
  – Gross hematuria (UA >50 RBC/HPF x 2)
  – CT scan and cystoscopy

• If history – negative
  – Renal and bladder US & KUB (done anyway!!!)
  – If radiographic studies abnormal- cystoscopy

Selective Endoscopic Surveillance 
High Risk Pt Populations

Colon Augmentation
  – 5% risk of colon cancer > 50yrs
  – 5% risk of cancer developing in colon augment in 50’s
  – Beginning screening at age 50 screen every 2-3 yrs

- Husmann & Rathbun J Ped Urology 2007
Selective Endoscopic Surveillance
High Risk Pt Populations

Immunosuppressives: post Tx
- Viral cystitis
- Yearly cysto’s beginning $\geq 10^{th}$ yr post Tx?


Selective Endoscopic Surveillance
High Risk Pt Populations

Exstrophy-Epispiadas
- History of prior urinary fecal mixing

Gastric Augments

- Malignancies in gastric augments
  - 12-15 yrs post op
- 2.8% per decade of F/U
  - Approx 2 times enteric augments
  - Atrophic gastritis -Bx – premalignant condition
  - Concern regarding composites (gastric-ileal)?


Conclusions

Patients with enteric augments can develop cancer!
Conclusion

Risk is low ~ 1.5% per decade
- 6-7 fold increase over normal population in the 6th decade of life
- However a etiology matched control population had a 3-4 fold increase over normal in the 6th decade of life
- Augment did not significantly increase the risk

Conclusions

Know the associations to cancer in augments
- Tobacco usage
- Immunosuppressives & viral cystitis
- Exstrophy (fecal-urine slurry)
- Gastric augmentations is a concern
**Balance**

- A problem yes, but let us **not over-react!!!**
- Let us **temper our response** with the benefit gained from the procedure
- Let us **not underestimate** the impact that urinary continence has on self esteem and social interactions

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**Mark Cain, not Twain**  
(But sage observations regardless!)

“…Finally, as these patients transition from a pediatric reconstructive practice to an adult urology practice, the specific long-term surveillance needs for those who have undergone augmentation cystoplasty need to be **better communicated to our colleagues in adult urology**, or as pediatric urologists we will need to provide long-term follow up for these patients into adult life. Since few pediatric urology practices have large enough numbers to identify an optimal protocol for screening this patient population, this follow up would present an ideal format for a much **needed multi-institutional prospective clinical study of cancer screening.**”
Risks & Benefits

Complex patients, who ½ a century ago had very high mortality rate & poor QOL
Goals (& expectations) are lofty: preserve renal status & obtain continence
• CIC
• Augmentation/outlet procedures
• Catheterizable stomas (urinary & MACE)
• Improved transplant anti-rejection protocols
What is the price of progress & facing the unforeseen??

“Only those who dare to fail greatly... can ever achieve greatly.”

- John F. Kennedy