SECTION ON UROLOGY

SCHEDULE

SATURDAY, OCTOBER 9, 1999

Section on Urology
8:00 am-4:45 pm
Room 38, Washington Convention Center

Session 1—Reconstruction

8:00 am
Podium 1
Decreased Linear Growth Associated With Intestinal Bladder Augmentation In Children With Bladder Exstrophy
Jennifer L. Dodson, MD; David-Alexandre C. Gros, MD; Uri A. Lapatin, John P. Gearhart, MD, FAAP; Richard I. Silver, MD; Steven G. Docimo, MD, FAAP. The Johns Hopkins Hospital, Baltimore, MD
Clinical Research Prize Finalist

8:05 am
Poster 2
Long Term Follow-up of the Hematuria-Dysuria Syndrome
J. Chadwick Plaire, MD; Warren T. Snodgrass, MD, FAAP; Michael E. Mitchell, MD, FAAP. Children’s Hospital, Seattle, WA

8:08 am
Poster 3
Seromuscular Sigmoidocystoplasty
F. de Badiola, E. Ruiz, J. Puigdevall, D. Caramatti, J. Molides, A. Sosa. Cirurgia Pediatrica, Hospital Italiano, Buenos Aires

8:11 am
Poster 4
Colococcal Bladder Augmentation with a Tapered Continent Ileal Limb: Use in the Neuropathic Bladder
D.A. Husmann, MD, FAAP; Mark Cain, MD, FAAP. Mayo Clinic, Rochester, MN

8:14 am
Poster 5
Stomal Stenosis: Is Ileum The Ideal Substitute For Efferent Limb Construction?
Martin Kaefer, MD; Richard C. Rink, MD, FAAP; Mark P. Cain, MD, FAAP; Anthony J. Casale, MD, FAAP; Riley Hospital for Children, Indianapolis, IN

8:17 am
Podium 6
Augmentation Ureterocystoplasty Could Be Performed More Frequently
Sasa V. Perovic, MD, PhD, FAAP; Vojkan Vukadinovic, MD; Miroslav Lj. Djordjevic, MD. Univeristiy Children’s Hospital, Belgrade, Yugoslavia

8:22 am
Discussion

8:38 am
Podium 7
“Co-Culture” of Bladder Smooth Muscle and Urothelial Cells on Small Intestinal Submucosa (SIS): Evaluation of the Best Culture Method for In Vitro Tissue Engineering Techniques
Y.Y. Zhang, MD; Bradley P. Kropp, MD, FAAP; Peter Moore, BS, MS; Rick Cowan, BS; Earl Y. Cheng, MD. University of Oklahoma, Oklahoma City, OK
Basic Research Prize Finalist

8:43 am
Podium 8
Regeneration of Functional Bladder Substitutes Using Large Segment (>44cm²) Acellular Matrix Allografts In A Porcine Model: Long Term Results
Premod Reddy, MD; Diego J. Barrieras MD; Darius J. Bagli, M.D.C.M., FAAP; Gordon A. McLorie MD, FAAP; Antoine E. Khoury MD, FAAP; and Paul A. Merguerian, MD, FAAP. Hospital for Sick Children, Toronto, ON Canada
Basic Research Prize Finalist

8:48 am
Podium 9
Enhancement Of Angiogenesis To Engineered Tissues Using VEGF Secreting Encapsulated Cells
Marcelle Machluf PhD; Gilad E. Amiel, MD; Shay Soker, PhD; Anthony Atala, MD, FAAP. Children’s Hospital, Boston, MA
Basic Research Prize Finalist

8:53 am
Poster 10
Comparison of the In Vitro Contractile Characteristics of Neuropathic and Normal Bladder Smooth Muscle Cells: Implications for Tissue Engineering
Earl Y. Cheng, MD; Rick Cowan, BS, Pete Moore, BS, MS; Y.Y. Zhang, MD; James J. Tomasek, PhD; Bradley P. Kropp, MD, FAAP. University of Oklahoma, Oklahoma City, OK

8:56 am
Discussion

Session 2—Bladder—Neurogenic

9:10 am
Podium 11
Transsection of Filum Terminale Remits Urinary and Stool Continence in Children with Neuropathic Bladder And Spina Bifida Occulta
Jeffrey S. Palmer, MD; Max Maizels, MD, FAAP; John A. Grant, MD, Ingrid Richards, RN; William E. Kaplan, MD, FAAP. Children’s Memorial Hospital, Chicago, IL

9:15 am
Podium 12
Erectile Dysfunction is a Treatable Condition in the Spina Bifida Male
Jeffrey S. Palmer, MD; William E. Kaplan, MD, FAAP; Casimir F. Firlit, MD, PhD, FAAP. Children’s Memorial Hospital, Chicago, IL
Clinical Research Prize Finalist

9:20 am
Poster 13
Sexuality Of The Spina Bifida Male And Female: Anonymous Questionnaires Of Function And Knowledge
Jeffrey S. Palmer, MD; William E. Kaplan, MD, FAAP; Casimir F. Firlit, MD, PhD, FAAP. Children’s Memorial Hospital, Chicago, IL

9:23 am
Discussion

9:32 am
Poster 14
Urologic Outcome of Patients with Cervical and Upper Thoracic Meningomyeloceles
Session 3—Hypospadias I

Moderators: A. Barry Belman, MD, and Warren Snodgrass, MD

10:25 am Podium 18
Modification of the Koyanagi Technique for Single Stage Repair of Proximal Hypospadias: Long Term Results
Haluk Emir, MD; Venkata R. Jayanthi, MD; Ken Nitahara, MD; Nur Danismand, MD; Stephen Koff, MD, FAAP. Children’s Hospital, Columbus, OH

10:30 am Poster 19
Radical Mobilization of the Bulbar Urethra to Lengthen Urethral Plane and Correct Chordee in Proximal Hypospadias
Linda A. Baker, MD; Ranjivo I. Mathews, MD; Steven G. Docimo, MD, FAAP. The Johns Hopkins Hospital, Baltimore, MD

10:33 am Poster 20
Results of Preputial Reconstruction in 77 Boys with Distal Hypospadias
Aart J. Klijn, MD; Pieter Dik, MD; Tom P. V. M. Delong, MD, FAAP. Wilhelmina Kinderziekenhuis, Utrecht, The Netherlands

10:36 am Discussion

10:45 am Poster 21
Anatomy of the Neurovascular Bundle: Is Safe Mobilization Possible?
Laurence Baskin, MD, FAAP; Priya Jathesan, MD; Ali Erol, MD; Wen Liu, MD; Yingguo Li, MD; Gerald Cunha, PhD. University of California, San Francisco, CA

10:48 am Podium 22
A Prospective Randomized Clinical Trial To Evaluate Methods Postoperative Care In Hypospadias
Gordon A. McLorie, MD, FAAP; Byron D. Joyner, MD, FAAP; Darius J. Bagli, M.D.C.M., FAAP; Jacques McCallum, RN; Paul A. Mercerian MD, FAAP; Antoine E. Khoury MD FAAP. Hospital For Sick Children, Toronto, Ontario, Canada

10:53 am Poster 23
Prospective Randomized Trial of Dressings Versus No Dressings in Hypospadias Repair
John C. Van Savage, MD; L. G. Palanca, MD; Bruce L. Slaughenhoupt, MD, FAAP. University of Louisville, Louisville, KY

10:56 am Poster 24
Urethral Seam Formation and Hypospadias
Priya Jagatheesan, MD; Laurence S. Baskin, MD, FAAP; Simon W. Hayward, Ph.D. and Gerald R. Cunha, PhD. University of California, San Francisco, CA

11:00 am Discussion

11:10 am AAP UROLOGY SECTION LECTURE

11:50 am LUNCH

Session 4—Bladder Function

Moderators: Ellen Shapiro, MD, and Anne-Marie Houle, MD

1:15 pm Podium 25
The Use Of Radiography, Urodynamic Studies And Cystoscopy In The Evaluation Of Voiding Dysfunction
Dipen J. Parekh, MD; John C. Pope IV, MD; Mark C. Adams, MD; John W. Brock III, MD, FAAP. Vanderbilt Children’s Hospital, Nashville, TN

1:20 pm Poster 26
Vasovagal Reactions in Children Suggest Autonomic Dysfunction in Dysfunctional Elimination Disorders
Andrej J. Combs, R.P.A.-C., Robert P. Weinstein, MD; Mark Horowitz, MD, FAAP and Kenneth I. Glassberg, MD, FAAP. Brooklyn, NY

1:23 pm Poster 27
Defunctionalized Bladders: Effects Before And After Refunctionalization
Marcos G. Machado, MD; James J. Yoo, MD; Anthony Atala, MD, FAAP. Children’s Hospital, Boston, MA

1:26 pm Podium 28
Diffusible Growth Factors Induce Bladder Smooth Muscle Differentiation
Laurence Baskin, MD, FAAP; Wen Liu, MD; Yingguo Li, MD; Simon Haywood, PhD; Gerald Cunha, PhD. University of California, San Francisco, CA

Basic Research Prize Finalist

1:31 pm Podium 29
Changing the Urothelial Phenotype: Abnormal Stromal-Epithelial Interaction
Laurence Baskin, MD, FAAP; Yingguo Li, MD; Wen Liu, MD; Simon Haywood, PhD; Gerald
Cunha, PhD. University of California, San Francisco, CA
Basic Research Prize Finalist

1:36 pm Discussion

1:55 pm Molecular Biology for Clinicians: Reading the Literature for Fun and Profit
Michael R. Freeman, PhD—Moderator
Laurence Baskin, MD—San Francisco
Darius Bågli, MD—Toronto
Anthony Atala, MD—Boston

2:50 pm Coffee Break and Poster Viewing

Session 5—Oncology
Moderators: Michael Ritchey, MD, and Duncan Wilcox, MD

3:10 pm Podium 30
Surgical Complications after Nephrectomy for Wilms Tumor: Report from the National Wilms Tumor Study Group (NWTSG)
M. Ritchey, MD, FAAP; R. Shamberger, MD, FAAP; G. Haase, MD, FAAP; J. Horwitz, MD; T. Bergmann, N. Breslow, PhD. The University of Texas Health Science Center, Houston, TX

3:15 pm Podium 31
Long Term Outcome Of Patients With Bilateral Wilms Treated With Renal Salvage Surgery
Rainer Kubiak, MD; Duncan T. Wilcox, FRCS; Patrick G. Duffy, FRCS; Phillip G. Ransley, FRCS, FAAP. Great Ormond Street Hospital for Sick Children, London, United Kingdom

3:20 pm Poster 32
A Control Release System Of Angiogenic Antagonists For Pediatric Tumor Therapy
Marcelle Machluf, PhD; Shay Soker PhD; Anthony Atala, MD, FAAP. Children’s Hospital, Boston, MA

3:23 pm Poster 33
Interleukin-8 (IL-8) and IL-8 Receptor Expression and IL-8 regulation In Human Neuroblastoma
Fernando A. Ferrer, MD; Lauri J. Miller, Patrick H. McKenna, MD, FAAP and Donald L. Kreutzler. Connecticut Children’s Medical Center, Hartford, CT

3:26 pm Discussion

Session 6—Bladder Obstruction
Moderators: Earl Cheng, MD, and Paddy Dewan, MD

3:40 pm Poster 34
Functional and Structural Changes in Guinea Pig Bladder Upon Urethral Obstruction
D.J. Kok, K.P. Wolffenbuttel, J. Minekus, R. Mastrigt, H. Vloedgraven, J.M. Nijman. Sophia Children’s Hospital, Rotterdam, The Netherlands

3:43 pm Poster 35
Bladder Outlet Obstruction—Influence on Sarcoplasmic Endoplasmic Reticulum Calcium Ion Pump (SERCA) Protein and Gene Expression
Raimund Stein, MD; Chaoliang Gong, PhD; Douglas A. Canning, MD, FAAP; Stephen A Zderic, MD, FAAP. Children’s Hospital of Philadelphia, Philadelphia, PA

3:46 pm Discussion

3:49 pm Poster 36
Heparin-Binding Epidermal Growth Factor-Like Growth Factor Expression is Induced in Bladder Smooth Muscle Tissue in Response to Passive and Active Contraction
Kathy G. Niknejad, MD; Hiep T. Nguyen, MD; Maryrose P. Sullivan, PhD; Lars J. Cisek, MD, PhD; Yalla V. Subbarao, M.D. and Craig A Peters, MD, FAAP. Children’s Hospital, Boston, MA

3:52 pm Podium 38
Mechanical Signals Activate Diverse Membrane Receptors Involved in Growth Factor Synthesis in Bladder Smooth Muscle Cells
Hiep T. Nguyen, MD; Samuel H. Bride, John M. Park, MD; Rosalyn M. Adam, PhD; Craig A. Peters, MD, FAAP; Michael R. Freeman, PhD. Children’s Hospital, Boston, MA
Basic Research Prize Finalist

3:57 pm Discussion

4:15 pm Poster 39
Neonatal Uterine Hypertrophy as a Cause for Temporary Bladder Outlet Obstruction in Infant Girls
Tom P.V.M. Dejong, MD, FAAP; Jan D. van Gool; Pieter Dik, MD; Aart J. Kijn, MD, Wilhelmina Kinderziekenhuis, Utrecht, The Netherlands

4:18 pm Poster 40
Does Neonatal Pyelo-Ureterostomy Worsen Bladder Function in Children With Posterior Urethral Valves
E. Jaureguizar, P. Lopez Pereira, MJ. Martinez Urrutia, R. Lobato, L. Espinosa. Hospital Infantil “La Paz”, Madrid, Spain

4:21 pm Poster 41
Improved Bladder Emptying In Posterior Urethral Valve Patients After Selective Alpha Blocker Therapy
Paul F. Austin, MD; Anthony J. Casale, MD, FAAP; Richard C. Rink, MD, FAAP. Riley Hospital for Children, Indianapolis, IN

4:24 pm Discussion

SUNDAY, OCTOBER 10, 1999

Section on Urology
6:45 am–5:00 pm
Room 38, Washington Convention Center

6:45 am–7:45 am
Instructional Review Course – Surgical Management Of Intersex Disorders
Richard Rink, MD, FAAP, and Richard Horwitz, MD, FAAP
Session 7—Exstrophy I

Moderators: Michael Mitchell, MD, and Paolo Caione, MD

8:00 am

Podium 42
The Newborn Exstrophy Bladder Too Small for Primary Closure: Evaluation, Management and Outcome
Jennifer Dodson, MD; Ilhami Surer, MD; Linda Baker, MD; John P. Gearhart, MD, FAAP. The Johns Hopkins Hospital, Baltimore, MD
Clinical Research Prize Finalist

8:05 am

Podium 43
Peri-Urethral Muscular Complex Identification and Reassembly in Exstrophy-Epispladias Repair: Rationale and Technique
Paolo Caione, MD; N. Capozza, MD; A. Lais, MD; E. Matarazzo, MD. Ospedale Pediatrico Bambino Gesu, Rome, Italy

8:10 am

Podium 44
Preliminary Experience With Neonatal Complete Primary Closure Of Exstrophy/Epispadias
Douglas E. Coplen, MD. St. Louis Children’s Hospital, St. Louis, MO

8:15 am

Podium 45
Management of Female Bladder Exstrophy/Epispadias with Total Urogenital Complex Mobilization
Bradley P. Kropp, MD, FAAP and Earl Y. Cheng, MD. University of Oklahoma, Oklahoma City, OK

8:20 am

Discussion

8:32 am

Poster 46
Bladder Matrix Changes in Exstrophy-Epispladias Complex. Developmental Defect or Acquired in Uterus?
Alberto Lais, MD; Guido Ciprandi, MD; Marina Frascarelli, Ennio Matarazzo, MD; Nicola Capozza, MD; Paolo Caione, MD. Ospedale Pediatrico Bambino Gesu, Rome, Italy

8:35 am

Poster 47
Clinical and Biomechanical Analysis of Hips in Adults with Bladder Exstrophy
M. M. Jani, B.A., Paul D. Sponseller, MD, FAAP; John P. Gearhart, MD, FAAP. The Johns Hopkins Hospital, Baltimore, MD

8:38 am

Poster 48
Determinates of Continence After Bladder Neck Reconstruction in the Bladder Exstrophy Population
David Y. Chan, MD; Robert D. Jeffs, MD, FAAP; John P. Gearhart, MD, FAAP. The Johns Hopkins Hospital, Baltimore, MD

8:41 am

Poster 49
The Modified Cantwell-Ransley Repair in Exstrophy and Epispadias: Ten Year Experience
Ilhami Surer, MD; Linda Baker, MD; Robert Jeffs, MD, FAAP; John P. Gearhart, MD, FAAP. The Johns Hopkins Hospital, Baltimore, MD

8:44 am

Discussion

Session 8—Reflex and Infection I

Moderators: H. Gil Rushton, MD, and Anthony Casale, MD

8:55 am

Podium 50
Tc-99m DMSA Renal Scan Abnormalities in Infants with Sterile, High Grade Vescoureteral Reflux
Hiep T. Nguyen, MD; Leonard Connolly, MD; Carol Barnewolt, MD; P.L. Ephraim, S. Ted Treves, MD; Craig Peters, MD, FAAP; Stuart B. Bauer, MD, FAAP. Children’s Hospital, Boston, MA
Clinical Research Prize Finalist

9:00 am

Poster 51
Neonatal Vescoureteral Reflux: Natural History
Waild Farhat, MD; Gordon McLorie, M.D. FAAP; GianPaolo Capolucchio M.D.C.M., Paul Merguerian MD, FAAP; Darius Bagli M.D.C.M., FAAP; Antoine Khoury MD, FAAP. Hospital for Sick Children, Toronto, ON, Canada

9:03 am

Poster 52
Treatment of Bladder Dysfunction in Infants with Dilating Vescoureteral Reflux
Ulla Sillen, MD; Marc Bacheralard, MD; Einar Hanson, MD; A-L. Hellstrom, MD; Ewa Solness, RN. Ostra Hospital, Goteborg, Sweden

9:06 am

Discussion

9:20 am

Poster 53
Is There a Risk of Contralateral Reflux After Primary Obstructive Megaueter Repair?
Paolo Caione, MD; L. Asili, MD; N. Capozza, MD; A. Lais, MD; E. Matarazzo, MD. Ospedale Pediatrico Bambino Gesu, Rome, Italy

9:25 am

Poster 54
Bilateral Extravesical Ureteroneocystotomy (Detrusorrhaphy) In Children: Limited Risk For Postoperative Urinary Retention
William R. Strand, MD, FAAP. Children’s Medical Center, Dallas, TX

9:28 am

Podium 55
Ketorolac Suppresses Postoperative Bladder Spasms After Intravesical Ureteral Reimplantation
John M. Park, MD; Constance S. Houch, MD, FAAP; Naveen F. Sethna, MD; Lorna J. Sullivan, RN; David A. Diamond, MD, FAAP; Anthony Atala, MD, FAAP, Joseph G. Borer, MD; Bartley G. Cilento, MD; Alan B. Retik, MD, FAAP; Stuart B. Bauer, MD, FAAP. Children’s Hospital and Harvard Medical School, Boston, MA
Clinical Research Prize Finalist

9:33 am

Poster 56
Are Post-operative Studies Justified after Extravesical Ureteral Reimplantation?
Diego Barriens, MD; Steven Lapointe, MD; Pramod P. Reddy, MD; Pierre Williot, MD, FAAP; Gordon McLorie, MD, FAAP; Darius Bagli MDCM, FAAP; Antoine E. Khoury, MD, FAAP; Paul A. Merguerian, MD, FAAP. Hospital for Sick Children, Toronto, ON, Canada

9:36 am

Discussion
9:50 am Coffee Break and Poster Viewing

Session 9—Laparoscopy

Moderators: Alaa ElGhoneimi, MD, and C.K. Yeung, MD

10:10 am Podium 57
Extraperitoneal Endoscopic Nephrectomy in Infants and Children
Prince Wales Hospital, Hong Kong, China

10:15 am Podium 58
Laparoscopic Retroperitoneal Nephrectomy in High Risk Children
Alaa El-Ghoneimi, M.D.; Louis Sauty, MD; Joel Maintenent, MD; Marie-Alice Macher, MD; Henri Lottmann, MD; Yoes Aigrain, MD.
Hospital Robert Debré, Paris, France

10:20 am Poster 59
Is Retroperitoneal Renal Biopsy an Alternative to Percutaneous Needle and Open Biopsies?
Paolo Caione, MD; S. Micali, MD; A. Lais, MD; E. Matarazzo, MD; N. Capozza, MD. Ospedale Pediatrico Bambino Gesù, Rome, Italy

10:23 am Podium 60
Laparoscopic Surgery In Children With Venticulopontineal Shunts Is Not Associated With Consequences Of Increased Intracranial Pressure
Stev G. Docimo, MD, FAAP. The Johns Hopkins Hospital, Baltimore, MD

10:28 am Poster 61
Nonpalpable Undescended Testis: Does the Order of Procedure Affect Outcome and Cost? A Prospective Randomized Analysis of Laparoscopy and Groin Exploration
Anthony J. Casale, MD, FAAP; Paul F. Austin, MD; Mark P. Cain, MD, FAAP; Martin Kaefer, MD; Richard C. Rink, MD, FAAP. Riley Hospital for Children, Indianapolis, IN

10:31 am Discussion

10:50 am American Urological Association Lecture
Dr. David Bostwick, MD, Richmond, Virginia

11:30 am AAP Section on Urology Medal Presentation
Dr. Robert D. Jeffs, MD, FAAP

11:45 am Business Meeting

12:15 pm LUNCH

Session 10—Reflux and Infection II

Moderators: Saul Greenfield, MD, and Francis Schneck, MD

1:30 pm Poster 62
Variability of Significance of Nuclear Medicine Cystogram
Khalid Fouda-Neel, M.D. and J.F. Shillinger, MD. Children’s Hospital of Eastern Ontario, Ottawa, Ontario, Canada

1:33 pm Poster 63
Should the Performance of the VCUG be Based on Race in the Evaluation of Prenatal Hydronephrosis?
Bartley G. Cilento, Jr., MD; Anthony Atala, MD, FAAP; Craig Peters, MD, FAAP; Stuart Bauer, MD, FAAP; Joseph Borer, MD; Robert L. Lebowitz, MD, FAAP; P.L. Ephraim; Natuwen Tu; Alan B. Retik MD, FAAP. Children's Hospital

1:36 pm Podium 64
Prediction of Outcome in the Management of Vescicoureteral Reflux: Role of Neural Networks
Satbir Singh, MD; Umesh Patil, MD, FAAP; Steven Docimo, MD, FAAP; Ranjit Mathews, MD, FAAP. University Hospital, Syracuse, NY and The Johns Hopkins Hospital, Baltimore, MD
Clinical Research Prize Finalist

1:41 pm Podium 65
Vescicoureteral Reflux Dysregulates the Renin-Angiotensin System in the Fetal Sheep Kidney
Samuel H. Bride, Hiep T. Nguyen, MD; Rita Gobet, MD; Craig A. Peters, MD, FAAP. Children’s Hospital, Boston, MA
Basic Research Prize Finalist

1:46 pm Poster 66
Congenital Vescicoureteral Reflux in Sheep is Associated with Reduced Expression Levels of Aquaporin-1 and Aquaporin-2 in Kidney Inner Medulla
Rita Gobet, MD; Lars Cisek, MD, Ph. D.; Craig A. Peters, MD, FAAP; Soren Nielsen, MD, PhD; Jorgen Frkaier, MD. University Children’s Hospital, Zurich, Switzerland and Children's Hospital, Boston, MA

1:49 pm Discussion

2:04 pm Podium 67
Expression Array “Gene Chip” Analysis of In Vitro Urethral Exposed to Uropathogenic Escherichia coli FDC1
R. W. Grady, MD; M. E. Mitchell, MD, FAAP, A. Mahmoudi; A. E. Stapleton, MD. Children’s Hospital, Seattle, WA
Basic Research Prize Finalist

2:09 pm Poster 68
The Induction Of Nitric Oxide Synthase In Human Bladder Smooth Muscle Cells By Inflammation: A Potential Mechanism For Fibrosis
Paul F. Austin, MD; Juan Wang, MS; Anthony J. Casale, MD, FAAP; Mark P. Cain, MD, FAAP; Martin Kaefer, MD; Richard C. Rink, MD, FAAP; Marco Chedid, PhD. Riley Hospital for Children, Indianapolis, IN

2:12 pm Poster 69
Growth Inhibition of E. coli by the Urine of Children with Urinary Tract Anomalies Under Prophylactic Antibiotics
O. Kessler, A. El-Khayam, L. Godfrey, B. Wolach, I. Nissenkorn, A. Pomeranz. Meir Hospital, Kfar-Saba, Israel

2:15 pm Discussion

2:30 pm Poster 66
Vescicoureteral Reflux: Point–Counterpoint (Jointly with the Section on Nephrology)
Moderator—Howard McC. Snyder, III, MD, FAAP, Billy Arant, MD, Philip Ransley, MD

3:10 pm Coffee Break and Poster Viewing

3:30 pm Pediatric Nephrolithiasis: A Hidden Disease
Session 11—Stone/Ureteroscopy

Moderators: Gregory Dean, MD, and Isreal Franco, MD

4:15 pm
Podium 70
Management of Distal Ureteral Stones in Children—Similarities to AUA Guidelines in Adults.
John G. Van Savage, MD; Lucio G. Palanca, MD; Robert D. Andersen, MD; Ganesh S. Rao, MD; Bruce L. Slaughenhaupt, MD, FAAP. University of Louisville, Louisville, KY

4:20 pm
Poster 71
The Ureteroscopic Treatment of Proximal Ureteral and Intrarenal Collecting System Calculi in the Pediatric Population
Michael Erhard, MD; Mark A. Barraza, MD, FAAP. Nemours Children’s Clinic, Jacksonville, FL

4:23 pm
Poster 72
Ureteropyeloscopy And Holmium Laser Lithotripsy For Upper Tract Calculi In Children
Mark A. Cabelin, MD; David Hoenig, MD; Gregory E. Dean, MD. Cooper Hospital, Camden, NJ

4:26 pm
Podium 73
Hypercalcemia and Stone Recurrence in Pediatric Urolithiasis
H. Norman Noe, MD, FAAP. Memphis, TN

4:31 pm
Discussion

4:45 pm
Podium 74
Long-Term Follow-up of Endoscopic Incision of Ureteroceles: Intravesical Versus Extravesical
Christopher S. Cooper, MD; Giacomo Passerini-Glazel, MD; Joel C. Hutcheson, MD; Massimo Iafrate, MD; Cristina Camuffo, MD; Claudio Milani, MD; Howard M. Snyder, III, MD, FAAP. Children’s Hospital of Pennsylvania, Philadelphia, PA

4:50 pm
Podium 75
Natural History of Reflux in Patients with Ureteroceles
R. Wayne Hatfield, MD; Martin Kaefer, MD; Richard C. Rink, MD, FAAP; John C. Pope, IV, MD; John W. Brock, III, MD, FAAP; Mark C. Adams. Vanderbilt Children’s Hospital, Nashville, TN and Riley Hospital for Children, Indianapolis, IN

4:55 pm
Poster 76
Endoscopic Puncture of Ureteroceles as Minimal Invasive and Long-term Effective Procedure in Children
Boris Chertin, MD; Alon Fridmans, MD; Irit Hadas-Halperin, MD; Wail Abu-Arefeh, MD; Moshe Zilberman, MD; Amicur Farkas, MD, FAAP. Shaare Zeder Medical Center, Jerusalem, Israel

4:58 pm
Discussion

MONDAY, OCTOBER 11, 1999

Section on Urology
6:45 am—4:15 pm
Room 32/33, Washington Convention Center

6:45 am—7:45 am
Master Class
Senior professors discussing cases, and focusing on the resident, fellow, and junior faculty level audience
Doug Canning, MD, FAAP, Moderator.
Howard Snyder, MD, FAAP
Alan Retik, MD, FAAP
Edmond Gonzales, MD, FAAP
John Woodard, MD, FAAP

Session 12—Kidney Obstruction

Moderators: George Steinhardt, MD, and Jorgon Frokiaer, MD

8:00 am
Podium 77
Symptomatic Ureteropelvic Junction Obstruction in Children in the Era of Prenatal Sonography—Is there a Higher Incidence of Crossing Vessels?
Mark P. Cain, MD, FAAP; Adam C. Thomas, Paul F. Austin, MD; Martin Kaefer, MD; Anthony J. Casale, MD, FAAP; Richard C. Rink, MD, FAAP. Riley Hospital for Children, Indianapolis, IN

8:05 am
Podium 78
The Long Term Follow-up of Newborn Hydronephrosis Initially Managed Non-Operatively.
Ibrahim Ulman, MD; Venkata R. Jayanthi, MD, FAAP; Stephen A. Koff, MD, FAAP. Children's Hospital, Columbus, OH

8:10 am
Podium 79
Renal Pelvis Histopathology Correlates with Radiologic Outcome Following Pyeloplasty in Children with UPJ Obstruction.
Peter D. Furness III, MD; Sang Won Han, MD; Max Maizels, MD, FAAP; Pauline M. Chou, MD; Sandra K. Fernbach, M.D. and Earl Y. Cheng, MD. Yonsei University, Seoul, Korea and University of Oklahoma, Oklahoma City, OK

8:15 am
Discussion

8:24 am
Poster 80
Renal Expression of HB-EGF Inhibits Mechanical Stretch-Induced Apoptosis in Collecting Duct Cells
Hiep T. Nguyen, MD; Samuel H. Bride, B.A., Rosalyn M. Adam, PhD; Jianquin Lin, Craig A. Peters, MD, FAAP; Michael R. Freeman, PhD. Children’s Hospital, Boston, MA

8:27 am
Poster 81
The Effect of Bradykinin Antagonist (HOE140) on Renal Parenchymal Injury Following Unilateral Ureteral Obstruction
Paul K. Pietrow, MD; John C. Pope IV, MD; Mark C. Adams, MD; John W. Brock III, MD,
8:30 am

Poster 82
Renal Function and Morphology in Experimental Unilateral Hydronephrosis: Are Early MRI Morphology or Renography Predictors of the Outcome?
Anni Eskild-Jensen, MD; Jørgen Frækiaer, MD; D.M.Sc.; Hans Tødkilde Jørgensen, MD; D.M.Sc.; Jens Christian Djurhuus, D.M.Sc.; Træls Munch Jørgensen, MD; D.M.Sc. Aarhus University Hospital, Aarhus, Denmark

9:15 am

Poster 89
Corporal Tissue For Penile Reconstruction
German Falke, MD; James J. Yoo, MD; Marcos G. Machado, MD; Robert Moreland, PhD; Anthony Atala, MD, FAAP. Children’s Hospital, Boston, MA

9:18 am

Poster 90
Construction of Female Urethra Using Buccal Mucosa Graft
John M. Park, MD; W. Hardy Hendren, MD, FAAP, FACS, FRCS(1). Children’s Hospital, Boston, MA

9:21 am

Poster 91
Results of Reconstruction of Children with High Urogenital Sinus
Moneer Hanna, MD, FAAP; Salima Al-Ramadan, MBCh, FRCS, Ibrahim Baaouy, MBCh, FAAP; Jeffrey Stock, MD, FAAP. New York Hospital-Cornell Medical Center, New York, NY, Children’s Hospital of New Jersey, Livingston, NJ

9:24 am

Podium 92
Initial Experience With the Transurethral Self Detachable Balloon System For Urinary Incontinence
David A. Diamond, MD, FAAP; Anthony Atala, MD, FAAP; Stuart B. Bauer, MD, FAAP. Children’s Hospital, Boston, MA

9:29 am

Discussion

9:45 am

Coffee Break and Poster Viewing

9:50 am

Session 14—Testis

Moderators: David Diamond, MD, and Stanley Kogan, MD

10:10 am

Podium 93
Placental Estradiol: A Purported Etiologic Factor of Human Cryptorchidism
F. Hadziselimovic, MD, FAAP; Geneto L.R. Emmons, PhD; Kinderarzt FMH, Liestal, Switzerland

10:15 am

Podium 94
Pretreatment Testicular Location: No Difference In Paternity Of Undescended Testis After Unilateral Cryptorchidism
Peter A. Lee, MD, PhD; Michael T. Coughlin, PhD; Mark F. Bellinger, MD, FAAP. Children’s Hospital of Pittsburgh, Pittsburgh, PA

10:20 am

Poster 95
DNA Organization in Patients with a History of Cryptorchidism
Joseph G. Barone, MD, FAAP; Kenneth B. Cummings, MD; Steven W. Ward, PhD. University of Medicine and Dentistry of New Jersey, New Brunswick, NJ

10:23 am

Poster 96
**Session 15—Hypospadias II**

Moderators: Mark Zaontz, MD, and Edward Reda, MD

- **3:00 pm**
  - Podium 102
  - How Efficient is the Prenatal Diagnosis of Ambiguous Genitalia
    - Y. Aigrain, MD; A. Cheikhelard, MD; E. Vuillard, MD; J. Léger, MD; M. Polak, MD; A. ELGhoneimi, MD. Hospital Robert Debré, Paris, France

- **3:05 pm**
  - Discussion

- **3:13 pm**
  - Podium 104
  - Snodgrass Hypospadias Repair Without Circumcision
    - Francisco deBadiala, MD; Alejandro Sosa, Juan Molides, Juan C. Puigdenou, Eduardo Ruiz. Hospital Italiano, Buenos Aires, Argentina

- **3:18 pm**
  - Poster 105
  - Histology Of The Urethral Plate: Implications For Hypospadias Repair
    - Warren Snodgrass, MD, FAAP; Kathleen Patterson, MD; Chad Plaire, MD; Richard Grady, MD; Michael Mitchell, MD, FAAP. Children's Hospital, Seattle, WA

- **3:21 pm**
  - Poster 106
  - The Gitup (Glanuloplasty and in Situ Tubularization Of The Urethral Plate ) Hypospadias Repair: A Simple Technique For Distal Hypospadias Repairs
    - Andrew K. Chung, MD; Evan J. Kass MD, FAAP. William Beaumont Hospitlal, Royal Oak, MI

- **3:24 pm**
  - Outcome Analysis of Tubularized Incised Plate Hypospadias Repair
    - Antoine E. Khoury, MD, FAAP; Alpana Prasad, MD; Paul A. Mergerian, MD, FAAP; Gordon A. McLorie, MD, FAAP; Darius J. Bagli, MDCM, FAAP. Hospital for Sick Children, Toronto, ON Canada

- **3:27 pm**
  - Poster 108
  - Management of Penoscrotal Transposition: A Novel Approach
    - Israel Franco, MD, FAAP; Mark Kolligian, MD; Edward F. Reda, MD, FAAP. Westchester Medical Center. Valhalla, NY

**Session 16—Exstrophy II**

Moderators: Curtis Sheldon, MD, and Enrique Jaureguizar, MD

- **3:50 pm**
  - Podium 109
  - Cloacal Exstrophy: Management Of The 46XY Genotype
    - J. Chadwick Plaire, MD; Michael E. Mitchell, MD, FAAP. Children's Hospital, Seattle, WA

- **3:55 pm**
  - Podium 110
804  SUPPLEMENT

Adult Clinical Psychosocial Adaptation in Patients Born with Bladder Exstrophy
H. Jauregizar, MD; M. J. Martinez Urrutia, P. Lopez Pereira, C. Soto, M. Diaz. Hospital Infantil “La Paz”, Madrid, Spain

4:00 pm  Poster 111
The Use of Pelvic Osteotomy in Repair of Bladder Exstrophy
Paul D. Sponseller, MD, FAAP; M. M. Jani, BA; John P. Gearhart, MD, FAAP. The Johns Hopkins Hospital, Baltimore, MD

4:03 pm  Poster 112
Results of Umbilicoplasty for Bladder Exstrophy
Christian Pavlovich, MD; Jeffrey Stock, MD, FAAP; Moneer Hanna, MD, FAAP. New York Hospital-Cornell Medical Center, New York, NY and Children's Hospital of New Jersey, Livingston, NJ

4:06 pm  Discussion

4:15 pm  ADJOURN

UNMODERATED POSTERS

1  The Role of Idiopathic Hypercalciuria in a Sub Group Of Dysfunctional Voiding Syndromes of Childhood
Dipen J. Parekh, M.Ch., John C. Pope IV, MD; Mark C. Adams, MD; John W. Brock III, MD, FAAP. Vanderbilt Children's Hospital, Nashville, TN

2  The Dysfunctional Voiding Scoring System (DVSS): Objective Criteria Evaluation Of Voiding Dysfunction in Children
Walid Farhat, MD; Darius J Bagli, MDCM, FAAP; GianPaolo Capollicchio, MDCM, Sheila O’ Reilly, RN, Paul A. Merguerian, MD, FAAP; Antoine Khoury, MD, FAAP; Gordon A. McLorie MD, FAAP. Hospital for Sick Kids, Toronto, Ontario, Can

3  Structural Changes In The Bladder Walls Of Pregnant And Hormone Treated Rats: Correlation To Bladder Dynamics
Larissa V. Rodriguez, Bingyin Wang, Steven P. Lapointe, Linda M. Dairiki Shortliffe. Stanford University, Stanford, CA

4  Is Proactive Clean Intermittent Catheterization Safe and Practical in Newborns with Spinal Dysraphism?
Jose M. B. Netto, MD; Luis M. Perez, MD, FAAP; David B. Joseph, MD, FAAP. Children’s Hospital of Alabama, Birmingham, AL

5  Outcome of Gastrocystoplasty in Tertiary Pediatric Urology Practice
Michael P. Leonard, MD, FAAP; Nafisa Dhramsi, MD; Pierre E. Williot, MD. Hospital Sainte-Justine, Montreal and Children’s Hospital, Winnipeg, Canada

6  In vitro engineering of human stratified urothelium: analysis of its morphology and functionality
Sita Sugasi, Yannick Lesbros, Isabelle Bisson, Pavel Kucera, MD; Peter Frey, MD, Bsc, FAAP. Centre Hospitalier Universitaire Vaudois and University Institute for Physiology, Lausanne, Switzerland

7  The Microbiology Of Bladder Augmentation In Children
Anthony J. Casale, MD, FAAP; Ronald S. Suh, Romano T. DeMarco, MD; Mark P. Cain, MD, FAAP; Richard C. Rink, MD, FAAP. Riley Children’s Hospital, Indianapolis, IN

8  Laparoscopic ACE (Antegrade Continence Enema) In Situ Appendix Procedure for Refractory Constipation and Fecal Incontinence in Children with Spina Bifida.
John G. Van Savage, MD; Paulos Yohannes, MD; Bruce L. Slaughenhoup, MD, FAAP. University of Louisville, Louisville, KY

9  Umbilicus Reconstruction in Patients with Bladder Exstrophy
Francisco deBadiala, MD; Juan C. Puigveaol, Alejandro Sosa, Juan Molides, Eduardo Ruiz. Hospital Italiano. Buenos Aires, Argentina

10  How Well Do Exstrophy Patients Actually Void?
Elizabeth B. Yerkes, MD; Mark C. Adams, MD; John C. Pope, IV, MD; Richard C. Rink, MD; John W. Brock, III, MD, FAAP. Vanderbilt Children’s Hospital, Nashville, TN

11  Avoidance of Inguinal Incision in Cases of Laparoscopically Confirmed Vanishing Testicle.
John G. Van Savage, MD; Bruce L. Slaughenhoup, MD, FAAP. University of Louisville, Louisville, KY

12  Pelvic Fracture Urethral Injuries In Female Children
Miguel L. Podesta, MD; Ricardo Medel, MD; Roberto Castera, MD; Marcela Herrera. Centro Medico San Luis, Buenos Aires, Argentina

13  Ureterocoele Disproportion (Non-Obstructive Ureteroceles) Revisited
John M. Park, MD; Stuart B. Bauer, MD, FAAP, David A. Diamond, MD, FAAP, Craig A. Peters, MD, FAAP, Anthony Atala, MD, FAAP, Alan B. Retik, MD, FAAP. Children’s Hospital, Boston, MA

14  The Use of Computerized Tomography (CT) in the Evaluation of Duplication Anomalies
Mark Horowitz, MD, FAAP; Ivan Colon, MD. Downstate Medical Center, Brooklyn, NY

15  Lower Urinary Tract Reconstruction for Non-Functioning Renal Moieties Associated with Ureterovesical Junction Pathology: A Review of Three Institutions’ Experience
Andreo C. Roberts, MD; Bradley P. Kropp, MD, FAAP; Earl Y. Cheng, MD; Kenneth A. Kropp, MD, FAAP; Thomas S. Parrott, MD, FAAP. University of Oklahoma, Oklahoma City, OK

16  Cost And Outcome Trends In Open Pyeloplasty: A Single Institution Five-Year Review
W. Barratt Gilbert, MD; John C. Pope IV, MD; Mark C. Adams, MD; John W. Brock III, MD, FAAP. Vanderbilt Children’s Hospital, Nashville, TN
Ischemia-Reperfusion Injury Induces Renal Tubular Cell Production of TNF-α
Kirstan K. Donnahoo, MD; Daniel R. Meldrum, MD; Zianzhong Meng, MD; Lihua Ao, Alfred Ayala, Ph.D.; Brian D. Shames, MD; Mark P. Cain, MD, FAAP; Aiden H. Harken, MD. Riley Children’s Hospital, Indianapolis, IN

A Modified Extravesical Ureteral Reimplantation Technique Using an “Inverted-Y” Detrusor Dissection
James O. L’Esperance, MD; Yegappan Lakshmanan; Leo C.T. Fung, MD. University of Massachusetts Medical Center, Worcester, MA

Double Onlay Preputial Flap For Hypospadias Repair: Experience With A New Technique in 46 Patients
Roman Jednak, MD; Ubinjarja Barroso Jr., MD; Julia Spencer Barthold, MD, FAAP, Ricardo Gonzalez, MD, FAAP. Children’s Hospital of Michigan, Detroit, MI

Long-Term Evaluation of Hypospadias Repair: Patient and Family Perspective of Functional and Aesthetic Results
Umesh Patil, MD, FAAP; Elan Salzhauer, Manjula Subramanian, Ranjite Mathews, MD, FAAP. Syracuse, NY

Free Grafts for Penile Curvature
Richard E. Caesar, MD; Anthony J. Caldamone, MD. Hasbro Children’s Hospital, Providence, RI

Bovine Pericardium as a Corporal Cavernoortal Patch Material in the Repair of Penile Chordee
Vernon M. Pais, MD; Yegappan Lakshmanan, MD; Leo C.T. Fung, MD. University of Massachusetts Medical Center, Worcester, MA

Ring Around The Penis: A Technique To Correct Severe Hypospadias And Lower The Risk Of Urethral Stricture Or Meatal Stenosis, Initial Results
Ross M. Dexter, MD, FAAP. Hershey Medical Center, Hershey, PA

Hypospadias Failure: Outcome Of Urethral Reconstruction In 36 Patients
Gianantonio Manzoni, Giacinto Marrocco, Ospedale di Circolo; S. Camillo Hospital, Rome, Italy

Management of Recalcitrant and Fulminating Venereal Wart Infections in Children with High Dose Cimetidine
Israel Franco, MD, FAAP. Westchester Medical Center, Valhalla, NY

Uroplakin And Androgen Receptor Expression In The Human Female Genital Tract: Insights Into The Development Of The Vagina In Normal Females And In Congenital Adrenal Hyperplasia
Ellen Shapiro, MD, FAAP; Hong-Ying Huang, MD; Xue-Ru Wu, MD. New York University Medical Center, New York, NY

Consensus On The Approach To Antenatally Detected Urologic Abnormalities
C.D. Anthony Herndon, MD; Patrick H. McKenna, MD, FAAP; Andrew L. Freedman, MD, FAAP; Fernando A. Ferrer, MD. Connecticut Children’s Medical Center, Hartford, CT

Outcome Analysis of Vesicoumniotic Shunt Insertion for Suspected Bladder Outlet Obstruction
Gordon A. McLorie, MD, FAAP; Mohammad Abdul-Aaly, MD; Antoine E. Khoury, MD, FAAP; Darius Bagli, M.D.C.M., FAAP; Paul A. Merguerian, MD, FAAP; Greg Ryan, MD; Denis Geary, MD. Hospital for Sick Kids, Toronto, Ontario, Canada

DECREASED LINEAR GROWTH ASSOCIATED WITH INTESTINAL BLADDER AUGMENTATION IN CHILDREN WITH BLADDER EXSTROPHY.

Jennifer L. Dodson, MD, David-Alexandre C. Gros, MD, Uri A. Lopatin, BA, John P. Gearhart, MD, FAAP, Richard I. Silver MD, Steven G. Docimo, MD, FAAP. Division of Pediatric Urology, Brady Urological Institute, The Johns Hopkins Hospital, Baltimore, MD.

Background: While some case series have suggested delayed linear growth after enterocystoplasty, none of these were case-controlled and the series did not necessarily include patients whose bladders were augmented for identical reasons. Therefore, the present study was performed to examine the hypothesis that intestinal bladder augmentation is associated with reduced linear growth.

Methods: Fifty patients who had undergone bladder augmentation for incontinence resulting from bladder extrophy were randomly selected from our institution’s patient data-base and matched for gender, age and type of extrophy with 50 non-augmented bladder extrophy patients. Patients were then contacted and asked to permit their pediatricians to release their growth charts. Once consent was obtained, the charts were requested from the pediatricians. Evaluative data (defined as at least one height pre and post augmentation) were obtained for 20 (40%) augmented and 14 (28%) non augmented patients. Results: The mean age at operation was 7.7 years. Delayed growth defined by a postoperative drop in percentile height occurred in 18 (90%) of augmented patients, with a mean loss of 17 percentile points. In the control group, delayed growth after 7.7 years of age occurred in 4 (29%) patients, with the control group as a whole gaining average of 8 percentile points. A Shapiro-Wilk test found the height to be normally distributed (p=0.19 and 0.93 respectively) and a t-test showed the mean height change to be significantly different between the two groups (p=0.006). The average follow up periods of 6 and 7.4 years in the augmented and non-augmented groups, respectively, were not significantly different (p=0.19). Conclusion: Intestinal bladder augmentation is associated with a nearly universal decrease in percentile height. Analysis of subtle metabolic alterations may provide information to help minimize or prevent growth impediment in the future. Alternatives to intestinal augmentation should continue to be pursued.

LONG TERM FOLLOW-UP OF THE HEMATURIA-DYSURIA SYNDROME.

J. Chadwick Plaire, MD, Warren T. Snodgrass, MD, FAAP, and Michael E. Mitchell, MD, FAAP Children’s Hospital and Regional Medical Center, Seattle, WA

Background: In pediatric bladder reconstruction, gastrocystoplasty has both advantages and disadvantages. A unique disadvantage is the Hematuria-Dysuria Syndrome (HDS). We previously described this syndrome as any of the following symptoms: bladder spasm; suprapubic, penile or periurethral pain; coffee
brown or gross hematuria without infections; skin excoriation; and dysuria without infections. Our initial enthusiasm for the routine use of stomach tissue in urinary reconstruction waned primarily because of the concerns regarding HDS. As a follow-up to our initial study, we evaluated the long term incidence and severity of HDS in a large group of patients.

Methods: The medical records of 78 patients who underwent gastrocystoplasty, with a minimum of 5 years of follow-up, were reviewed. Follow-up data within the past year was available in 72 patients. The charts were examined to determine which patients currently have symptoms of HDS and any therapy required. Diagnosis included myelomenigoecele (28), bladder exstrophy (21), cloacal exstrophy (8), posterior urethral valves (6), sacral agenesis (3), pelvic tumor (2), bilateral ectopic ureters (2), non-neurogenic neurogenic bladder (1) and persistent cloaca (1). The average age at the time of gastrocystoplasty was 8.75 years and follow-up ranged from 5 years to 10 years.

Results: When using the broadest criteria of HDS, 17 (23%) patients were identified who had at least 1 of the above symptoms. However, only 3 patients (2 bladder exstrophy, 1 cloacal exstrophy) require medications on a daily basis to control symptoms of the HDS. One patient, who had posterior urethral valves, required removal of the gastric patch secondary to suprapubic pain and parental concern. Four patients require medications intermittently to control symptoms and the other 9 patients' symptoms are mild and self-limiting. The diagnosis of the patients with symptoms included bladder exstrophy (10), myelomenigoecele (2), posterior urethral valves (2), sacral agenesis (1), pelvic tumor (1), and cloacal exstrophy (1). Of the 17 patients with symptoms, 10 described suprapubic discomfort or dysuria alone, 5 described hematuria alone, and 2 described both dysuria and hematuria.

Conclusion: HDS is a unique disadvantage seen in patients undergoing gastrocystoplasty. In this large group of patients, with a minimum of 5 years follow-up, 23% describe some component of HDS. However, in only 5.5% (4/72) of patients the symptoms were severe enough to require constant medical therapy or surgical removal. A higher percentage of the patients with bladder exstrophy (10/21 or 47%) demonstrated symptoms when compared to the other groups of patients. Even though we raised the initial concerns with HDS, we feel that gastrocystoplasty continues to be an excellent alternative in pediatric bladder reconstruction. The severity of HDS does not appear to be a major problem in the majority of patients in the long term and therefore should not deter one from using gastric tissue.

3 SEROMUSCULAR SIGMOIDCYSTOPLASTY


Background and Objectives: Intestinal bladder augmentations have well recognized complications including mucus production, metabolic abnormalities and perforations. These complications might be avoided if the intestinal mucosa is not incorporated into the urinary tract. Here we report our experience with seromuscular sigmoidcyoplasty (SSC) including clinical, urodynamic and histological results.

Materials and Methods: We performed SSC in 19 of 130 patients undergoing bladder augmentation. There were 10 males. The mean age was 8.7 years (2-19). Fourteen patients had neurogenic bladder, 2 anorectal malformations, 2 bladder exstrophy and 1 posterior urethral valves. The indications for augmentation were poor bladder compliance with urinary incontinence and/or hydronephrosis. Complete follow up urodynamic data are available for 16 patients (mean 8 months). In 10 patients, endoscopic biopsies of the augmented segment were obtained. The operation consisted of opening the bladder sagittally and adding to it a reconfigured segment of sigmoid colon from which the mucosa had been removed preserving the muscularis mucosa.

Results: All patients are dry on intermittent catheterization at four hour intervals or greater. There were no clinical urinary tract infections. Mucus production was not a problem and bladder irrigations were not necessary in any case. Capacity and compliance improved in all cases. Three patients presented periastatic contractions. Capacity increased from 87.3ml (30-300) to 333ml (200-400). Mean postoperative compliance was 17.4ml/cm (5-40). There was little or no mucus present on centrifuged urine specimens. Biopsies from 10 patients obtained 1 year after surgery revealed that the seromuscular layer of the sigmoid was now covered with pseudostratified epithelium with colonic glands but without crypts, probably representing metaplasia of the regrown colonic epithelium. The only complication seen in some patients has been prolonged hematuria, not clinically significant. This has been avoided in the last three cases by treating the demucosalized segment with the argon beam laser, a procedure that appears to further eliminate residual colonic glands.

Conclusion: The procedure described is simpler to perform than other similar ones that preserve the urothelial lining. The clinical and urodynamic results have been very satisfactory.

4 COLOCECAL BLADDER AUGMENTATION WITH A TAPERED CONTIENT ILEAL LIMB: USE IN THE NEUROPATHIC BLADDER

DA Husmann MD, FAAP, Rochester, MN and Mark Cain MD, FAAP, Indianapolis, IN

Background: In pts with a neurogenic bladder (NGB) needing a bladder augmentation use of a detubularized colocolic patch with a tapered ileal segment as a continent catheterizable stoma has generally been disregarded as an option due to concerns regarding fecal continence.

Methods: A retrospective review of pts with a NGB managed by a colocolic bladder augmentation using a continent tapered ileal limb was performed. All pts included in this study had failed conservative management with anticholinergic medications and intermittent catheterization. To be considered for this procedure all patients had to have documented fecal continence prior to the operation.

Results: A total of 63 pts were managed by this technique. The neurologic defect was caused by a spinal cord injury in 42, myelodysplasia in 18 and sacral agenesis in 2. All pts had a simultaneous bladder outlet obstructive procedure, 42 had rectus fascial slings and 21 had bladder neck closure. Reasons for simultaneous bladder neck closure were vesicovaginal fistulas in 9, vesicocutaneous ulcer fistulas in 7 and erosion of an AUS into the bladder neck in 5. The ileal cecal valve was chosen as the continent mechanism due to the absence of the appendix in 16 (26%) and the surgeons preference in 46 (74%). The surgical procedure resulted in 1 perioperative death (1.5%) due to an PE. Complete urinary continence was achieved at the time of the original surgery in 54/62 pts (88%), 4 (6%) had diurnal and nocturnal incontinence per stoma and 4 (6%) had only nocturnal incontinence per stoma. All of the continent pts received peristomal continence injections, four (50%) became continent. Of the persistently continent pts 2/25% have undergone open surgical revision to become continent, and 2 (25%) have persistent incontinence. In total 60/62 (97%) pts are completely continent. Upper tracts were preserved in 58 pts (94%), 3 pts (4.5%) developed progressive bilateral hydronephrosis due to noncompliance with catheterization, and 1pt (1.5%) developed progressive unilateral hydronephrosis due to development of a ureteral stricture. Fecal continence was improved (less problems with constipation) in 14 (23%), unchanged in 46 (74%) and worse in 2 (3%). Both pts with deterioration in bowel function were routinely continent of feces but noted significant soilage with antibiotic usage. Overall additional surgery was necessary in 36
(58%) pts, during a median follow-up interval of 6 years, range 1–9 yrs. The need for additional surgery was, removal of bladder calculi in 16 (26%), stomal procedure for continence 8 (14%), stomal stenosis 4 (6%) rupture of the augment 4 (6%), SBO 2 (3%), parastomal hermia 1 (1.5%), and ureteral obstruction 1(1.5%).

Conclusion: In selected pts with a NGB colocolic bladder augmentations with a tapered ileal stoma will provide excellent urinary continence, preserve the upper tracts and does not routinely result in fecal incontinence.

5

STOMAL STENOSIS: IS ILEUM THE IDEAL SUBSTRATE FOR EFFERENCE LIMB CONSTRUCTION?

Martin Kaefer, MD, Richard C. Rink, MD, FAAP, Mark P. Cain, MD, FAAP and Anthony J. Casale, MD, FAAP. Department of Urology, Indiana University Medical Center, Indianapolis, IN.

Background: Construction of the efferent conduit can be the most challenging aspect of continent urinary diversion (CUD). Complications involving the catheterizable channel have been reported in up to 30% of patients, with stomal stenosis being one of the most common. We report the incidence of stomal stenosis relative to the biomaterial used for efferent limb construction.

Methods: We retrospectively reviewed the records of all patients undergoing the creation of a continent catheterizable channel from 1985 to 1997. In cases where appendix (N=46), Bladder–continent vesicostomy (N=22), or reconfigured ileum–Monti technique (N=14) was utilized, the stomal site was created using a laterally based V-flap of skin. In cases where tapered ileum was employed (N=10), the stoma was brought flush to the skin. All ileal conduits were constructed over a 12–14 Fr. catheter. Presenting diagnosis, date of operation, interval to stomal stenosis and other complications involving the CUD construction were recorded. Patients with less than one year of follow up were excluded from further analysis (N=11).

Results: Stomal stenosis occurred in 19 of 92 patients (20%) with the majority occurring during the first year of follow up (11/19 = 58%). Stenosis requiring surgical revision occurred most frequently when appendix or a bladder flap were utilized (10/46 and 9/22, respectively: average interval to stenosis = 1.4 years, range: 2 months–6 years). In contrast, this complication was not appreciated in patients with efferent conduits constructed from reconfigured ileum (Monti or Tapered) (p<0.0001). Stomal location was not a predictor of stomal stenosis (Umbilicus 10/49 = 20% vs. Lower Quadrant 7/34 = 20% vs. Neumobilius 2/9 = 20%).

Conclusion: Efferent conduits constructed from ileum have had a significantly lower incidence of stomal stenosis in our series when compared to appendiceovesicostomy and continent vesicostomy. We would strongly recommend the use of ileum when utilizing strategies that require a bowel Anastomosis (i.e. ileal augmentation). We would tend to favor a Monti ileovesicostomy over appendiceovesicostomy in all other situations although the Monti follow up is relatively short.

<table>
<thead>
<tr>
<th>Biomaterial</th>
<th>Incidence</th>
<th>Time to Stenosis (avg.)</th>
<th>Follow-up (avg.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendiceovesicostomy</td>
<td>10/46</td>
<td>19 months</td>
<td>3.4 years</td>
</tr>
<tr>
<td>Continent Vesicostomy</td>
<td>9/22</td>
<td>13 months</td>
<td>3.0 years</td>
</tr>
<tr>
<td>Ileum—Tapered</td>
<td>0/10</td>
<td>NA</td>
<td>8.1 years</td>
</tr>
<tr>
<td>Ileum—Monti</td>
<td>0/14</td>
<td>NA</td>
<td>1.3 years</td>
</tr>
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</table>

6

AUGMENTATION URETEROCYSTOPLASTY COULD BE PERFORMED MORE FREQUENTLY

Sava V. Perovic, MD, PhD, FAAP (Affiliate), Voikan Vukadinovic, MD and Miroslav Li. Djordjevic, MD. Dept. of Urology, University Children’s Hospital, Belgrade, Yugoslavia.

Background: Gastrointestinal segments are most often used for bladder augmentation. However, there are numerous complications related to their incorporation into the urinary tract. Megaureters represent the ideal tissue, but ureterocystoplasty has been used only in selected cases up to now. Our effort was to show that it could be used more frequently by using the distal part of the megaureter for augmentation and proximal one for reinplantation.

Methods: From November 1995 to September 1998 ureterocystoplasty was performed in 16 patients, aged 3 to 12 years (mean 6.6). In 9 pts with impaired renal function loop ureterocystoplasty was previously done to preserve and improve renal function. Distal part of ureters was dilated by balloon catheters. In the remaining 7 pts bladder augmentation and simultaneous ureteroneocystostomy were performed without ureterocystoplasty. Ureterocystoplasty was done extraperitoneally. Distal part of megaureter was used for augmentation. For constructing the bladder of adequate shape, bladder expander was inserted during surgery and removed two weeks later. Proximal part of the megaureter was mobilized and implanted into the bladder using extravasal detrusor tunneling ureteroneocystostomy.

Results: Follow up was from 6 to 41 months (mean 23 months). The new increased bladder capacity ranged from 296ml to 442ml (mean 371ml) for both groups. Compliance was improved in all cases with decrease of number of CIC per day. There was no further worsening of the renal function. Transitory VUR was noted in three patients without clinical symptoms.

Conclusion: Megaureter presents the ideal tissue for bladder augmentation. Division of the ureter and using its distal part for augmentation is always possible. Augmentation ureterocystoplasty performed in this way could be done more frequently.

7

“CO-CULTURE” OF BLADDER SMOOTH MUSCLE AND UROTHELIAL CELLS ON SMALL INTESTINAL SUBMUCOSA (SIS): EVALUATION OF THE BEST CULTURE METHOD FOR IN VITRO TISSUE ENGINEERING TECHNIQUES

Y.Y. Zhang, MD, Bradley P. Kropp, MD, FAAP, Peter Moore BS, MS, Rick Cowan, BS, and Earl Y. Cheng, MD. Department of Urology, Children’s Hospital of Oklahoma and University of Oklahoma, Oklahoma City, OK.

Background: Small intestinal submucosa (SIS) is a xenogenic, acellular, collagen rich membrane with inherent growth factors previously shown to promote in vivo bladder regeneration and support the individual 3 dimensional growth of bladder smooth muscle cells (SMC) and urothelial cells (UC). It is currently unknown whether in vitro seeding of SIS with cells will enhance the regeneration process and what the best method of seeding is for use with this technique. This study was conducted to evaluate the combined in vitro growth of SMC and UC on SIS and to determine the best culture method for in vitro tissue engineering use.

Methods: Primary cultures of bladder SMC and UC were established from both humans and dogs using standard explant techniques. The following cell culture experiments were then carried out with both dog and human cells individually. Cultured cells were seeded on SIS at a density of 1x10^5 cells per cm^2 SIS, incubated, and harvested at 3, 7, 14 and 28 days. Four separate groups were studied: 1) UC seeded alone on the mucosal surface of SIS, 2) SMC seeded alone on the mucosal surface, 3) "co-culture": SMC and UC seeded simultaneously on the mucosal surface, and 4) "sandwich" culture:

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SMC seeded on serosal surface followed by seeding of UC on the mucosal surface 24 hours later. The SIS-cell constructs were formalin fixed at the time of harvesting and processed for routine histology including Masson's trichrome staining. The specific cell growth characteristics were studied with special attention to cell morphology, cell proliferation, cell adherence, and 3 dimensional patterns of growth. To help in the identification of cells in the groups where cells were seeded together, immunohistochemical analysis was performed with antibodies to smooth muscle α-actin and cytokeratins AE1/AE3.

Results: Both human and dog cells grew similarly on SIS. When seeded alone, SMC and UC grew in several layers with minimal matrix penetration. When cells were seeded on the SIS in "co-culture", there appeared to be a synergistic effect with respect to enhanced growth and penetration of the SIS membrane. Both SMC and UC layered more readily and had greater adherence to the SIS. Cells formed a thick stratified layer that was organized such that SMC were basally located with matrix penetration while the UC grew in multiple layers with early polarity on top of the proliferating SMC. With the "sandwich technique" there was also enhancement of growth and penetration, however this was less pronounced when compared to the "co-culture" technique. Cell growth was progressive over the 28 day period of observation with the majority of proliferation occurring in the first 14 days. Immunohistochemical studies demonstrated that both SMC and UC maintain the expression of the phenotypic markers of differentiation (smooth muscle α-actin and cytokeratins AE1/AE3).

Conclusions: SIS is capable of supporting the differentiated growth of human and dog bladder cells in vitro. The present study suggests that the co-culture method of seeding provides the best bladder graft material for in vitro tissue engineering techniques. Additionally, this study demonstrates that there are important smooth muscle-epithelial cell interactions involved in the enhancement of in vitro growth of bladder cells. This in vitro model will be a valuable tool for the future study of these critical interactions and the cellular signals involved in the process of tissue regeneration. These results also have important implications for the future clinical use of tissue engineered bladder grafts for urinary tract reconstruction.

8

REGENERATION OF FUNCTIONAL BLADDER SUBSTITUTES USING LARGE SEGMENT (>44 CM²) ACELLULAR MATRIX ALLOGRAFTS IN A PORCINE MODEL: LONG TERM RESULTS

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Introduction and Objectives: We have previously presented the short-term (4 wks) results of a morphometric analysis of a bladder acellular matrix allograft (BAMA) bioprosthesis using segments >24 cm². We demonstrated BAMA repopulation of native bladder cell phenotypes throughout the entire thickness of the allograft. We now present long term (12 wks) morphometric as well as functional outcomes of BAMA integration into porcine bladders, utilizing large segments measuring >44 cm² (mean surface area).

Methods: BAMA was prepared by detergent and enzymatic extraction of porcine bladders, to achieve an acellular matrix. Eighteen pigs had partial (≥50%) cystectomies performed and then BAMA segments were implanted onto their bladders, average size 44 cm² (max size 72 cm², n=6). No urinary diversion was employed. The animals were then sacrificed at 1 wk (n=2), 2 wks (n=2), 4 wks (n=2), 8 wks (n=3) and 12 wks (n=9). The native bladder and repopulated BAMA segment were stained with Hematoxylin-Phloxine-Saffron and immunohistochemistry staining for Collagen I & III, α-actin, Cytokeratin-7, Protein gene product 9.5 and Acetyl-Choline (to demonstrate in vivo functional nerve endings). The samples were analyzed morphometrically with light and con-focal microscopy to evaluate cellular repopulation and matrix re-organization. Videourodymatic studies were performed at monthly intervals in the 8 and 12 wk preps, to evaluate bladder capacity, compliance and emptying ability, as well as radiographic morphology.

Results: All animals survived the surgical procedure and there were no urinary leaks. None of the animals developed urinary calculi or hydro nephrosis. At 1 wk there was a diffuse infiltration with acute inflammatory cells. Isolated areas of smooth muscle cell (SMC) infiltration of the BAMA were noted. At 2 wks the luminal BAMA surface was lined with a single layer of urothelium, Stromal infiltration with non-organized SMC and evidence of angiogenesis in the deeper BAMA regions. At 4 wks the urothelium was multi-layered with organizing groups of SMC and discrete blood vessel lumens noted. By 8 and 12 wks, the SMC formed well-defined muscle bundles, and there was a cellular repopulation of nerve sheaths extending throughout the entire thickness of the BAMA allograft. Upto 4 wks the regeneration of BAMA occurred with a centripetal decrease in cell density. However by 8–12 wks a considerable (catch-up) increase in central cell density was observed. Videourodymatic studies demonstrated that the regenerated bladders had capacity (max 300 cc) and compliance comparable to native bladders, without demonstrating any uninhibited contractions or persistent elevations of bladder filling pressures. Moreover, BAMA allograft bladders showed gross structural symmetry, without any adynamic segments visualized radiographically.

Conclusions: We present evidence that large patch BAMA allograft implantation is technically feasible. The advantages of BAMA include the potential for cellular and functional regeneration of a bladder substitute, including neural regeneration, while avoiding the complications associated with conventional bladder augmentation strategies. Bladder acellular matrix allograft (BAMA) may prove to be a viable surgical alternative to bladder augmentation with intestinal segments.

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ENHANCEMENT OF ANGIogenesis TO ENGINEERED TISSUES USING VEGF SECRETING ENCAPSULATED CELLS

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Introduction: One of the major obstacles facing tissue engineered organs and tissues is inadequate vascularization of the implants. Poor vascularization limits the transport of nutrients and oxygen to the seeded cells, and may result in tissue necrosis. Angiogenesis, the process of new blood vessel formation, is regulated by different molecules, such as vascular endothelial growth factor (VEGF). In the present study renal cells seeded on acellular matrices were implanted in mice followed by injection of alginate-PLL encapsulated Chinese hamster ovary (CHO) cells, expressing VEGF (CHO/VEGF). The encapsulation of CHO/VEGF enables the long term release of VEGF while isolating the CHO/VEGF cells from the host immune system.

Methods: VEGFα2 cDNA was subcloned into an expression vector that was used to transfect CHO cells and high VEGF secreting cells were selected. CHO/VEGF cells were suspended in sodium alginate solution and extruded into a CaCl2 solution where they gelled and were further coated with poly-L-lysine. The encapsulated cells were cultured and the medium was changed every week and assayed for VEGF using western blotting analysis. Unencapsulated cells were used as controls. A mixture of cultured renal cells harvested from 5 days old mice were seeded on a biological acellular matrix. Subsequently, 48 cell-seeded matrices were implanted subcutaneously in 24 nude mice. Twenty four hours later, alginate-PLL microspheres containing CHO/VEGF
cells were injected to 12 mice, near the area of implantation. Renal units of the study and control groups (i.e. with and without the injected alginate) were harvested 3, 7 and 20 days after implantation.

Results: Western blot analyses performed on conditioned media taken from encapsulated cells revealed extended amount of VEGF protein when compared to non encapsulated cells. High levels of VEGF were maintained for 6 weeks in culture. Macrosopic examination of mice injected with encapsulated cells together with the implant, revealed a progressive increase in vascularization at the implanted sites. In contrast, the control group which was not injected with CHO/VEGF cells, did not demonstrate enhanced vascularization. Immunohistochemical analysis of VEGF and VEGF receptors showed positive staining of vessels. An increased number of capillaries and blood vessels was observed when compared to the control group.

Conclusions: These results indicate that extensive amounts of VEGF are released from encapsulated CHO/VEGF cells in vitro and in vivo. The release of VEGF in vivo greatly stimulated vascularization in the area of the implant. This new approach can be used to enhance vascularization of tissue engineered implants.

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COMPARISON OF THE IN VITRO CONTRACTILE CHARACTERISTICS OF NEUROPATHIC AND NORMAL BLADDER SMOOTH MUSCLE CELLS: IMPLICATIONS FOR TISSUE ENGINEERING

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Background: It has recently been demonstrated that cells can be cultured from the normal animal bladder in vitro, seeded on a biodegradable matrix, and then placed back into the host to induce regeneration of near normal bladder. Clinically, cells utilized in tissue engineering techniques such as this will not be derived from a normal bladder. They will usually come from a neuropathic bladder with abnormal contractile properties. It is unknown whether neuropathic bladder cells in vitro will retain their abnormal contractile characteristics or whether they will revert back to a normal pattern. This study compares the in vitro contractility of neuropathic bladder smooth muscle cells (SMC) and cells cultured from the normal bladder.

Methods: Primary cultures of bladder SMC were established utilizing standard explant techniques from patients with a neuropathic bladder (n=3, urodynamically with poor bladder compliance and poor contractility) undergoing augmentation and from patients with a normal bladder (n=5) undergoing ureteral reimplantation. Cells from passage 5 were seeded on 1% collagen lattices (150,000 cells/lattice) and cultured for 5 days in M199 media with 10% serum. Contractility of the SMC–lattice constructs were then analyzed following exposure to a panel of well known contractile agonists including: 10% serum, Ca-Ionophore (1 μM), and lymphosporadic acid (LPA) (1 μM). Total contraction (mean % reduction of the original lattice diameter) and relative contraction (% reduction of the lattice as compared to reduction obtained with 10% serum) were measured at the 10 minute time point.

Results: Neuropathic bladder SMC had significantly less total contraction to 10% serum (20% less as compared to the contraction obtained with normal bladder SMC, p ≤ .05), Ca-Ionophore (50% less than normal, p ≤ .05), and LPA (47% less than normal, p ≤ .05) (see figure 1). There was no significant difference in the total contraction obtained in serum free conditions between neuropathic and normal bladder SMC (p >.05). Interestingly, the relative contraction to all of the agonists was not significantly different when neuropathic and normal bladder SMC were compared (p >.05).

Conclusions: These results demonstrate that cultured neuropathic bladder SMC promote a significantly weaker contractile response when compared to cultured normal bladder SMC. However, both types of cultured cells maintain a similar agonist profile. The clinical implications of these findings with respect to whether these cells will continue to retain these functional differences when utilized in tissue engineering techniques to promote bladder regeneration requires further investigation.

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TRANSECTION OF FILUM TERMINALE REMITS URINARY AND STOOL CONTINENCE IN CHILDREN WITH NEUROPATHIC BLADDER AND SPINA BIFIDA OCCULTA

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Background: Children with day/night wetting, urine infection, and enuresis are difficult to treat. In children with spina bifida occulta (SBO), recent evidence suggests that traction of the filum terminale on the caudal spinal cord may be causing this dysfunction. Transection of the filum terminale has been reported to improve continence. Herein we report our experience with transection of the filum terminale for such children.

Methods: From a group of about 500 children who have been evaluated since 1994 for a combination of day and/or night wetting, urinary tract infection, and enuresis, we identified a cohort of 8 children (girls=5, boys=3) who: 1) did not respond to conventional treatment (enuresis alarms, pharmacotherapy, diet, and psychological treatment); 2) manifested SBO; 3) showed neurogenic bladder despite a normal neurological examination and MRI; and 4) normal urological examination including cystoscopy. The effectiveness of the procedure was determined by assessing the postoperative resolution of enuresis and stool incontinence.

Results: There were 8 children (mean age of 9.5 years) who fulfilled the criteria and had filum terminale transection. By 6 months postoperatively, all children had complete resolution of the nocturnal enuresis and stool incontinence; diurnal enuresis was completely resolved (57%) or markedly improved (43%). Complications from the operation occurred in only one girl who experiences back pain.

Conclusion: Transection of the filum terminale is an effective treatment modality for select children with refractory urinary and/or bowel incontinence, namely those who show spina bifida occulta and abnormal urodynamic testing despite a normal MRI.

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ERECTILE DYSFUNCTION IS A TREATABLE CONDITION IN THE SPINA BIFIDA MALE

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Background: Now that individuals with spina bifida live well into adulthood, erectile dysfunction has become a recognized associated medical disorder. Surprisingly, no study has dealt specifically with the treatment of erectile dysfunction in spina bifida males. Therefore, we conducted a prospective, blinded, randomized, placebo-controlled, dose-escalation, crossover study to determine the ability to treat erectile dysfunction in spina bifida men with sildenafil citrate (Viagra).

Methods: Fourteen males (18 years of age and older) with spina bifida and a clinical diagnosis of erectile dysfunction were assigned to take 4 sets of tablets (5 tablets per set) in a random order. All men took 25mg and 50mg of sildenafil citrate and 2 identical-looking sets of corresponding placebos 1 hour before planned sexual activity. Efficacy was assessed by the effect of treatment compared to baseline (i.e. before treatment): 1) rating of erections (scored from 0 to 10); 2) duration of erections; and, 3) frequency of erections and confidence to obtain an erection based on response to questions 1 and 15 (scored from 0 to 5 and 1 to 5, respectively) of the International Index of Erectile Function, respectively. Statistical analysis was performed with a p-value <0.05 considered statistically significant. The Food and Drug Administration exempted this protocol from the requirements of Part 312 of the IND regulations.

Results: Eleven men (79%) reported improved erectile function while on sildenafil compared to both baseline and placebos. There was a significant dose-dependent improvement of erectile function with both 25mg and 50mg of sildenafil compared to baseline (p<0.05): 1) mean erectile score increased by 54% and 89%, respectively; 2) mean duration of erections increased by 199% and 271%, respectively; 3) mean frequency of erections increased by 65% and 100%, respectively; and, 4) mean level of confidence increased by 33% and 67%, respectively. Furthermore, 50mg of sildenafil provided greater improvement in all 4 parameters compared to 25mg. In comparison, the placebo results were not significantly different compared to baseline for any of the parameters.

Conclusion: This is the first study specifically demonstrating that erectile dysfunction in the spina bifida male is a medically treatable condition. Sildenafil citrate (Viagra) can be an effective therapy in this patient population and it improves their level of sexual confidence. Funded by a research grant from Pfizer, Inc.

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SEXUALITY OF THE SPINA BIFIDA MALE: ANONYMOUS QUESTIONNAIRES OF FUNCTION AND KNOWLEDGE
Jeffrey S. Palmer, MD, William E. Kaplan, MD, FAAP, and Casimir F. Firlit, MD, PhD, FAAP. Division of Urology, Children’s Memorial Medical Center, Northwestern University Medical School, Chicago, IL.

Background: Major advances have markedly increased the life expectancy of spina bifida individuals well into adulthood. As a result, erectile dysfunction has become a well-recognized associated medical disorder. The purpose of this study was to conduct the first anonymous evaluation of the sexual function and knowledge of these males.

Methods: All male patients 18 years of age and older from our Spina Bifida Center were mailed both: 1) the International Index of Erectile Function (IIEF) questionnaire; and, 2) a questionnaire designed by this study group: IIEF addresses the erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction. Our questionnaire evaluates: 1) rating of erections on a scale from 0 to 10; 2) duration of the erections; and, 3) knowledge of the sexual and reproductive capabilities of individuals with spina bifida. Both questionnaires were mailed back to the investigators anonymously. The protocol was approved by our institutional review board. Statistical analysis was performed with a p-value <0.05 considered statistically significant.

Results: 57 men (range: 18–61 years old) completed the questionnaires (32% response rate). The median erectile score was 6 (range: 0–10) with a median duration of rigidity of 5 minutes (range: 0–60 minutes). Only 9 (16%) had ever had a health professional initiate a conversation about sex. None of the 26 patients with erectile dysfunction had ever been treated for this condition. There was an inverse relationship (p<0.05) between the level of physical disability and: 1) the importance of sex to them; 2) level of sexual activity; 3) total score, erectile function score, orgasmic function score, sexual desire score, intercourse satisfaction score, and overall satisfaction score of the IIEF; and, 4) knowledge of the reproductive capabilities of individuals with spina bifida. In addition, significant racial differences were noted on the IIEF (p<0.05), with non-white males reporting a lower: 1) total score; 2) orgasmic function score; 3) sexual desire score; and, 4) overall satisfaction score than white males.

Conclusion: The results of these anonymous questionnaires reflect the need to educate, initiate conversations on sex, and treat spina bifida males with erectile dysfunction, with special attention paid to differences in physical disability and race. Funded by research grants from Pfizer Inc. and Mentor Medical Inc.

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UROLOGIC OUTCOME OF PATIENTS WITH CERVICAL AND UPPER THORACIC MENINGOMYELOCELES
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Background: Little information exists concerning the voiding dysfunction and risk for upper tract deterioration of patients born with cervical or upper thoracic meningomyeloceles (MMC). The spinal level of the vast majority of children born with meningomyeloceles occurs in the lower thoracic and lumbo-sacral regions. Children born with a cervical or upper thoracic level meningomyelocele constitute 1 to 5 percent of the entire meningomyelocele population. These children are typically ambulatory, and in theory they have a less hostile dynamics of their neurogenic bladder and lower risk to upper tract deterioration than children with lower level MMC.

Methods: We reviewed the neurosurgical and urological presentation, evaluation and management of 14 consecutive patients who had cervical (n = 11) or upper thoracic (n = 3) meningomyeloceles. There were 10 female and 4 male patients ages 10 months to 39 years of age (mean 12 years). All patients were ambulatory, and 8 of 14 (57%) had hydrocephalus. Although all patients had a voiding history obtained by a neurosurgeon, only 9 patients had formal urological evaluation including history, physical examination, and renal-bladder imaging studies. Six patients underwent video-urodynamic studies.

Results: Voiding dysfunction (mild incontinence) was noted in 2 of the 9 patients 5 years of age or older. No patient had increased post void residuals and none had ever been placed on intermittent catheterization. Only 1 patient had a history of urinary tract infections and this same patient was the only in the series on anticholinergic pharmacotherapy. Imaging studies of the upper tracts was normal in all 9 patients. Video-urodynamics was normal in 5 of 6 patients. One patient had mild hyperreflexia. One of 10 patients had vesicoureteral reflux despite normal urodynamic parameters. No patient has required urologic surgical intervention.

Conclusions: To our knowledge, this represents the largest reported series of patients with cervical and upper thoracic meningomyeloceles who have undergone urologic evaluation. Our limited experience suggests that patients with cervical and upper thoracic meningomyeloceles have a low risk of voiding dysfunction and upper tract deterioration. Additional reports of children with cervical and upper thoracic meningomyeloceles are necessary to confirm these findings.
INTRAVESICAL BLADDER STIMULATION IN PEDIATRIC PATIENTS WITH SPINAL CORD DEFECTS

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Background: Creating a low pressure continent urinary storage mechanism for the pediatric patient with a neurogenic bladder is a difficult problem. The current answer, enterocystoplasty with intermittent catheterization, is not an ideal solution. In an effort to optimize storage we used intravesical electro-bladder stimulation for patients with spinal cord defects.

Methods: A retrospective review of all pediatric patients with neurogenic bladders undergoing bladder stimulation was performed. Indications and goals of treatment were noted. Bladder stimulation was performed in the manner previously described by Kaplan. Parameters reviewed included patient age, initial age adjusted pressure specific (<30cm H2O) bladder volume (%PSBV), initial random urinary residual, number of treatments, number of sessions per treatment, follow-up %PSBV, voiding and continence status.

Results: Records were reviewed for all 44 patients treated. Initial age at initiation of therapy was 6.6 years. Indications included decreasing bladder storage pressures (n=24), increase continence between caths (n=13) and achieving volitional voiding (n=7). The first sessions averaged 18 treatments, the second 8.5, the third 7.6 and the fourth, 7.4 treatments.

<table>
<thead>
<tr>
<th>Indication</th>
<th>N</th>
<th>Initial PSBV%</th>
<th>Final PSBV%</th>
<th># Achieving Goal</th>
<th>% Achieving Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dec. Storage Pressure</td>
<td>24</td>
<td>0.48 ± 0.07</td>
<td>0.54 ± 0.06</td>
<td>3</td>
<td>13%</td>
</tr>
<tr>
<td>Dry between cath.</td>
<td>13</td>
<td>0.58 ± 0.09</td>
<td>0.71 ± 0.1</td>
<td>1</td>
<td>8%</td>
</tr>
<tr>
<td>Volitional voiding</td>
<td>7</td>
<td>0.9 ± 0.2</td>
<td>0.8 ± 0.2</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Patients who became dry had similar age at initiation of treatment, bony defect level, initial capacity and PVR, and number of treatments compared to non-responders. Non-responders required surgical intervention to achieve continence with safe storage pressures. One patient became incontinent after undergoing treatment to achieve volitional voiding.

Conclusion: While some high-risk patients were spared surgery with intravesical electro-bladder stimulation, most were not. Spontaneous voiding to completion, at safe pressures, was not achieved in this group of patients. We were unable to clarify, prior to treatment, which patients would benefit from this labor-intensive therapy.

ELECTRICALLY STIMULATED DETRUSOR MYOPLASTY

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Background: Many children with spina bifida and other causes for neurogenic bladder rely on clean intermittent catheterization to empty their hyporeflexic or areflexic bladders. Direct bladder and sacral nerve root stimulation have met with limited success. We study the electrical stimulation of a rectus abdominis muscle flap wrapped around the bladder to achieve bladder contractility and emptying.

Methods. The rectus abdominis muscle was surgically dissected with preservation of its insertion on the pubis bone and rotation of its midsection behind the bladder to effect a complete bladder wrap. The deep inferior epigastric artery and veins and the two lowermost intercostal nerves were preserved. This unilateral rectus abdominis muscle flap was then electrically stimulated with two pairs of bipolar electrodes inserted into the muscle near the entrance of the nerves. Stimulation frequencies of 40, 60 and 80 hertz were used in each of 8 dogs. The increase in bladder pressure over baseline, half time to muscle fatigue, and percent bladder evacuation were measured. Paired students T-tests were used for statistical comparisons.

Results. (Mean ± SEM) Although half-time to muscle fatigue was different for the 3 stimulation frequencies (p < 0.05), the increase in bladder pressure and % bladder evacuation were similar (p > 0.05).

Conclusions. The electrically stimulated detrusor myoplasty results in uniform increases in detrusor pressure and reasonable bladder evacuation in animal model. We are currently studying a detrusor myoplasty in a chronic study to determine whether it can be used for enhanced bladder emptying in children with poor detrusor contractility.

<table>
<thead>
<tr>
<th>Stimulation frequency (Hz)</th>
<th>40</th>
<th>60</th>
<th>80</th>
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<tbody>
<tr>
<td>Increase bladder pressure (cmH2O)</td>
<td>35 ± 5</td>
<td>45 ± 6</td>
<td>45 ± 7</td>
</tr>
<tr>
<td>Half-time to muscle fatigue (sec)</td>
<td>47 ± 6</td>
<td>33 ± 4</td>
<td>19 ± 4</td>
</tr>
<tr>
<td>Bladder evacuation (%)</td>
<td>73 ± 8</td>
<td>78 ± 8</td>
<td>74 ± 6</td>
</tr>
</tbody>
</table>

Supported by a grant from the Alliant Trust Fund, a non-profit organization.

URODYNAMIC PROFILE OF MYELODYSPLASTIC CHILDREN WITH SPINAL CLOSURE IN UTERO

Jeffrey Holzbeierlein, MD, John C. Pope IV, MD, Mark C. Adams, MD, Joseph Bruner, MD, Noel Tulipan, MD, and John W. Brock III, MD, FAAP. Divisions of Pediatric Urology, Pediatric Neurosurgery, and Maternal/Fetal Medicine, Vanderbilt University Medical Center, Nashville, Tennessee.

Background: Spinal dysraphism is the most common cause of neurogenic bladder dysfunction in newborns. Urodynamic findings in these children include uninhibited bladder contractions, bladder areflexia, decreased compliance, and detrusor sphincter dyssynergia. Early urodynamic studies in patients with spina bifida is recommended to help identify those with bladder characteristics that place them at risk for upper tract deterioration. A new intervention employing closure of the neural tube defect in
utero has recently been investigated at our institution in 25 patients. The supposition is that this procedure produces decreased exposure of the spinal cord to the amniotic fluid, which may improve neurologic function. To date, we have studied 16 of these patients with video urodynamics and compared the results to those reported in the literature on myelomeningocele patients without fetal intervention.

Methods: Sixteen patients with a mean age of 6.5 months (range 2-12 months) have undergone urodynamic testing including cystometrogram, fluoroscopic evaluation of filling and voiding, voiding cystourethrogram, and need for catheterization, the number of urinary tract infections, and medications were reviewed.

Results: Six percent of these patients demonstrated uninhibited detrusor contractions while 43% had an areflexic bladder. Nineteen percent demonstrated decreased compliance, and 75% had leak point pressures greater than 40 cm of H2O. Mean bladder capacity was 40 cc with 31% of patients having a much lower capacity than expected for age. Two patients had evidence of upper tract dilatation on previous renal ultrasounds; 2 had evidence of reflux on VCUG; 2 required intermittent catheterization; 1 required anticholinergic therapy; and 1 patient experienced a significant urinary tract infection.

Conclusion: The urodynamic findings in this population are comparable to those previously reported in the literature for patients with spina bifida without prenatal closure of the spinal defect. Our lower incidence of urinary tract infections and reflux probably represents more aggressive early urologic management of these patients rather than neurologic improvement. These urodynamic studies were performed very early in life and future evaluation may ultimately reveal improvement in bladder function when compared to other myelodysplastic patients. At this time, however, we recommend that patients with in utero closure of their spinal cord defect be evaluated and treated in the same manner as myelomeningocele patients without fetal intervention.

MODIFICATION OF THE KOYANAGI TECHNIQUE FOR SINGLE STAGE REPAIR OF PROXIMAL HYPSPADIAS: LONG TERM RESULTS

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Aim of the Study: To describe our modification on the Koyanagi technique for one stage proximal hypospadias repair and present long-term results.

Clinical Material: The modified technique was used to treat 20 patients with proximal hypospadias. Age at operation ranged from 7.5 months to 28 months old (mean = 12.9 months). In all cases, the urethral meatus was at or proximal to the penoscrotal junction. No patient had previously undergone penile surgery.

Surgical Technique: The Koyanagi procedure involves the use of bilateral meatal based skin flaps which course obliquely around the penile shaft and incorporate the inner layer of the prepuce to create the neourethra. As originally described by Koyanagi and used by others, these meatal-based flaps are created in such a manner as to receive their entire blood supply from the region around the urethral meatus. Our modification involves enhancing flap vascularity and providing neourethral covering by preserving the entire vascular supply to each flap by developing a lateral pedicle to each flap. Joining these pedicles together in the midline creates a vascularized second layer of covering for the neourethra.

Results: Postoperative follow up ranges from 11 to 69 months with a mean of 32.9 months. Pinhole urethrocystaneous fistulas developed in 4 patients (20%). There were no cases of meatal stenosis or urethral stricture. Cosmetic and functional results were excellent.

Conclusion: Our modification of Koyanagi's technique places great emphasis upon careful preservation of the underlying blood supply to the skin flaps and increasing vascularized neourethral covering. This is reflected in a relatively low complication rate for proximal hypospadias repair. We continue to prefer this technique for severe hypospadias because it avoids entirely a proximal anastomosis, which reduces the likelihood for proximal stricture formation. Meatal stenosis has also been eliminated by creating a 20F caliber meatus.

RADICAL MOBILIZATION OF THE BULBAR URETHRA TO LENGTHEN URETHRAL PLATE AND CORRECT CHORDDE IN PROXIMAL HYPSPADIAS

Linda A. Baker, Baltimore, MD Ranjiv I. Mathews, Syracuse, NY, and Steven G. Docimo, Baltimore, MD. (Presented by Dr. Baker)

Background: Reconstruction of children with scrotal or perineal hypospadias is a technically challenging procedure that is often performed in a staged fashion. Staging is often required to correct chordee and significant disproportion between the length of the dorsal corpora cavernosa and the urethral plate. Described is an alternative approach to one-stage correction wherein the ventral chordee was straightened and the urethral plate was lengthened by proximally mobilizing the normal bulbar urethra to or beyond the perineal body.

Methods: All patients presenting with proximal hypospadias from August 1997 to March of 1999 were included in this study. The surgical technique involved penile degloving with preservation of the urethral plate, followed by radical mobilization of the intact urethra to or beyond the perineal body. Penile chordee was then assessed and if present, was managed with dorsal plication sutures or dermal grafting of ventral corporotomies. If the urethral plate was intact with a straight penis, a tubularized, incised plate urethroplasty was performed to correct the hypospadias in one-stage. Otherwise, a two-stage repair was performed.

Results: Nine patients underwent the procedure with a mean age at operation of 11.5 months (range 172-710 days). Three patients had multiple congenital anomalies and two patients had bilaterally nonpalpable testes. Preoperatively, the meatus was perineal in two, midscrotal in six, and penoscrotal in one. Five patients had a bifid scrotum, one had a cleft scrotum and one had complete penoscrotal transposition.

After proximal urethral radical mobilization, penile straightening was complete in two of the nine cases, yielding either a glanular urethral meatus or a penoscrotal meatus. In four of the nine cases, penile straightening was achieved with proximal urethral mobilization and simple dorsal plication sutures, yielding a midshaft(1) or penoscrotal(3) meatus. In the remaining three patients, despite this aggressive proximal urethral mobilization and dissection between the urethral plate and corpora, completely separating these structures, the penis was not straight and therefore the urethral plate was divided. Chordee was straightened in one patient by dorsal plication sutures and the remaining two required dermal grafting of ventral corporotomies.

A simultaneous tubularized, incised plate urethroplasty was then performed upon the 4 penoscrotal and 1 midshaft meatus and this repair was covered with a deepithelialized vascular flap. Results of the six patients with successful one-stage procedures have shown an excellent cosmetic result and no fistulae at mean length of follow-up of 6.3 months (range 6-457 days).

Conclusion: Radical mobilization of the urethra proximal to the hypospadic meatus can be used to compensate for significant urethral tethering and chordee in a subpopulation of patients with
RESULTS OF PREPUTIAL RECONSTRUCTION IN 77 BOYS WITH DISTAL HYPOSTAPIAS

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Aims: The goal in hypospadias repair is the reconstruction of a normal penis in function and in appearance. Because of this we often get a request from parents to reconstruct the foreskin in boys referred for hypospadias repair. However the foreskin reconstruction can introduce an extra risk of stenosis, fistula or dehiscence, requiring an extra operation. We report the results of foreskin reconstruction in a group of 77 boys with distal hypospadias operated between 1990 and 1997.

Patients and Methods: 77 boys, mean age 24 months (range 6 months-13 years) had a distal shaft or coronal hypospadias repair with reconstruction of the foreskin. The majority of the boys was operated using a modified Mathieu technique. The prepucce was closed in three layers using interrupted vicryl 6.0 or 7.0 sutures. All patients were operated under antibiotic prophylaxis. Distal shaft urethral reconstructions were all treated with an indwelling catheter for 3 or 4 days and a compress for the same period.

Results: During the mean follow-up of 2 years (range 3 months-8 years) of the 77 boys, 52 (67%) obtained a cosmetic and functional optimal result. 25 Boys (33%) needed a second operation because of a fistula in the foreskin reconstruction (n=16 (21%),) or a combined problem with a fistula from urethra to skin and a foreskin dehiscence (n=7 (9%)), or a solitary problem of a fistula from the urethra to the skin without any problem with the reconstructed foreskin (n=2 (3%)). In the second operation of 3 boys we performed a circumcision on request of the parents, in the other 20 boys the fistula or dehiscence was closed in daycare.

All of the fistula presented in the first 3 months after the operation. No secondary phimosis was developed during follow-up.

Discussion: The 33% failure rate of the distal hypospadias repair with prepucce reconstruction is discouraging, at least when compared to the much lower failure rate of repair with a circumcision. One argument in favour of the reconstruction is that it preserves foreskin to be used in a possible second procedure to close a fistula or dehiscence.

Conclusion: The reconstruction of the prepucce introduces a 25-28% extra risk for a reoperation. We leave the acceptance of this risk to the parents. Our first choice is circumcision.

ANATOMY OF THE NEUROVASCULAR BUNDLE: IS SAFE MOBILIZATION POSSIBLE?

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Introduction: We have previously defined the anatomy of the neurovascular bundle in the normal and hypospadic penis. The most striking feature is the absence of nerves at the 12:00 o’clock position and the extent of neuro innervation not just at the 11:00 and 1:00 o’clock position but completely around the corporal bodies. Historical experience suggest that mobilization of the neurovascular bundle is anatomically possible. The goal of this study is to prove whether mobilization of the neurovascular bundle is safe and theoretically sound. Specifically; 1) Does the neurovascular bundle send perforating branches into the corporal bodies? 2) How far lateral does the dissection need to be, before nerves are injured and 3) Exactly how deep into buck fascia must one go?

Methods: Normal human fetal penile specimens (N = 35; gestational age 8 to 35 wks) and three hypospadiac specimens (30-41 wks) were serially sectioned and stained with Masson’s trichrome and the neuronal markers PGP 9.5 or S100. Computer reconstruction using Abode Photoshop and NIH imaging allowed three dimensional analysis of the nerves, corporal bodies and glans.

Results: (1) Perforating nerves into the erectile bodies were not documented along the dorsal or lateral aspect of the tunica in any of the specimens studied. Only in the area of the crus bodies on the ventral lateral surface were nerves noted to pierce into erectile tissue. (2) The neural network was extensive from the 11:00 and 1:00 position to the 5:00 & 7:00 position corresponding to the junction of the erectile tissue and urethral spongiosum. At this junction minor nerve branches were noted to perforate into the urethral spongiosum. (3) A microscopic plain exist between the neurovascular bundle and the tunica of the corporal bodies measuring between 30 and 50 microns in the specimens greater than 30 wks gestation.

Conclusion: Perforating branches from the dorsal-lateral neurovascular bundle into the erectile bodies do not exist based on serial step sectioning and microscopic examination of male genital specimens. Surgically it is possible to elevate the neurovascular bundle however the dissection needs to start at the junction of the urethral spongiosum and corporal bodies and remain directly on top of the tunica albugenia to prevent neuronal injury. Small perforating branches into the urethral spongiosum may be injured with unknown significance. We continue to advocate plication in the nerve free zone at 12:00 for the correction of penile curvature.

A PROSPECTIVE RANDOMIZED CLINICAL TRIAL TO EVALUATE METHODS POSTOPERATIVE CARE IN HYPOSTAPIAS

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Background: A prospective randomized clinical trial assessed the impact of various postoperative dressings on the burden of postoperative care in hypospadias. We hypothesize that a plan of management involving no dressing will achieve comparable healing and patient/parent comfort to that seen with the use of dressings.

Methods: Over a 14-month period, 120 boys (average age 2.2 yrs) underwent primary one-staged hypospadias repairs. The study was conducted at a single centre, with four surgeons participating. The repairs included both proximal (n=60), and distal (n=60) defects. All studies were done in an ambulatory setting. Following Ethical review, and informed consent, patients were randomized to receive one of three dressings (None/Tegaderm/Coban). All were interviewed and counselled by a Urology Nurse both before and immediately following surgery. The parents were asked to complete and return a questionnaire. The outcomes were compared, with respect to the need for repeat procedures, surgeon, and type of repair. The parents’ comfort in their care for the child at home as defined by the questionnaire, was analyzed with respect to the dressing, and the type of repair. The anticipated sample size to achieve the power to show anticipated differences was achieved, and a binomial statistical test was used to test the significance of the different outcomes (p=0.05).

Results: A total of 116 patients completed the study (three withdrawn by surgeon). Only one patient failed to complete the questionnaire. The postoperative regime did not correlate with the need for a repeat surgical procedure, nor did the type of procedure (Proximal, 16%, Distal 10%). The two dressings were associated
with more calls to MD’s or nurses (P>0.05), and more visits to health facilities than the “no dressing” group. The removal of the dressings caused a significant degree of patient discomfort to children, and concern to parents. Early bathing seemed associated with more patient comfort, and had no effect on wound healing.

Conclusion: Dressings do not provide significant benefits following hypospadias surgery of all types with respect to both wound healing and patient comfort. Parents and children appear happier in the postoperative period, when no dressings are employed. There is less burden of care, and effective wound healing, using a regime of no dressing following hypospadias surgery.

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PROSPECTIVE RANDOMIZED TRIAL OF DRESSINGS VERSUS NO DRESSINGS IN HYPOSPADIAS REPAIR

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Background: Dressings following hypospadias repair have the benefits of gentle compression for hemostasis, immobilization of the wound, and a “hermetic seal”. They have the disadvantages of producing possible ischemia, infection, and pain during the removal process. We compare the success and complications of hypospadias repair with and without dressings in a prospective randomized fashion.

Methods: Children with hypospadias were randomized either to receive or not receive a clear plastic dressing for two days. A written informed consent was obtained. Seventy-seven consecutive patients underwent hypospadias repair. Exclusion criteria were known coagulopathy (n = 0) and oozing at the end of the case (n = 2). Criteria for success were a glanular meatus, single forward directed stream, unimpeded voiding, absence of penile chordee, and good cosmesis. Statistical significance was considered when p was < 0.05.

Results: Between the dressed and non-dressed groups, randomization of the following parameters was successful: Fresh versus redo cases, position of the urethral meatus, severity of chordee, use of epinephrine, time of surgery, type of surgery, and type of chordee correction (p > 0.05). Forty of 42 patients (95%) had a successful result in the dressed group. One patient developed bleeding in the recovery room which resolved spontaneously. Two patients had mental regression. Thirty of 33 patients (91%) without a dressing had a successful repair. Five patients had bleeding in the recovery room which resolved spontaneously. Two patients had urethrocuntaneous fistulae, one of which resolved spontaneously. One patient with scrotal hypospadias had some redundant skin after a one-stage repair, which was trimmed for cosmetic purposes. The mean follow-up was one year. There was no statistical difference between the dressed and non-dressed groups with regard to success of the operation (p > 0.05).

Conclusion: There was no marked difference in the success rate for hypospadias surgery performed with or without a dressing. Use of dressings for hypospadias surgery remains at the discretion of the operating surgeon.

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URETHRAL SEAM FORMATION AND HYPOSPADIAS

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Introduction: The etiology of hypospadias remains elusive. During development of the proximal urethra in humans the urethral folds fuse to create a tubular urethra. The residual epithelial seam subsequently disappears. The mechanism of urethral seam removal has not been described. We hypothesized two possible mechanisms for urethral seam removal: (1) epithelial-mesenchymal transformation similar to palatal shelf formation and /or (2) apoptosis of the epithelial seam. To test these ideas we studied urethral development in the embryonic mouse genital tubercle.

We first documented that urethral development in the mouse involves fusion of the urethral folds and epithelial seam formation, as occurs in the human. We then studied the mechanism of epithelial seam removal.

Methods: Genital tubercles from embryonic male mice (15 to 20 days gestation) were removed, fixed in formalin and processed to paraffin. Six µm sections of the tissue were cut using a microtome. Serial sections were stained using immunocytochemical techniques for H&E, terminal transferase nuclear end labeling (TUNEL), and using antibodies to cytokeratins, smooth muscle α-actin and vimentin.

Results: H&E staining of serial sections showed the presence of a urethral plate which canalizes to form the urethral groove. Fusion of the urethral folds bounding the groove forms the urethra and a transient midline epithelial seam. This seam forms and disappears in a narrow band (approximately 30µm wide) of apoptotic activity. This region from which the seam was disappearing contained pyknotic nuclei which exhibited TUNEL staining. No evidence was seen of co-expression of cytokeratin and mesenchymal markers (actin or vimentin) thus excluding the possibility of epithelial to mesenchymal transformation.

Conclusions: Urethral seam formation occurs in both the mouse and the human. Our data in the mouse supports the hypothesis that epithelial seam removal occurs via apoptosis. Specifically, the disappearance of the epithelial seam occurred concurrently with a highly focalized wave of apoptotic activity suggesting a band of apoptosis which migrates distally along the penile shaft during development to complete the isolation of the penile urethra within its surrounding stroma. No evidence of cells co-expressing epithelial and mesenchymal markers was seen suggesting that an epithelial to mesenchymal transformation does not occur in the mouse penis.

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THE USE OF RADIOGRAPHY, URODYNAMIC STUDIES AND CYSTOSCOPY IN THE EVALUATION OF VOIDING DYSFUNCTION

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Background: Children with dysfunctional voiding disorders are often subjected to radiologic, cystoscopic or urodynamic evaluations in an effort to find an anatomic or organic cause. Our objective was to determine the role of the above investigations in the evaluation, management and ultimate outcome of a large patient population with voiding dysfunction from within a single institution.

Methods: 858 patients with dysfunctional voiding disorders seen from 1991 to 1998 were evaluated retrospectively. A thorough history and physical with specific emphasis on voiding patterns was elicited and uranalysis performed in all patients. Ultrasound of the urinary system was performed in 808 patients (94%) with 19 (2.2%) patients undergoing IVP. VCUG was performed in 480 patients (56%), 407 of which had a history of urinary tract infection. Cystoscopy was performed in 43 patients (5%) and a formal urodynamic study was performed in 26 (3%). Behavioral therapy was practiced in 620 patients (72%), 395 patients (46%) received antibiotics, 380 patients (44%) received anticholinergics, 135 patients (16%) were placed on bowel regulation regimen for concomitant bowel elimination problems and 53 patients (6.5%) were simply observed.

Results: Mean age at referral was 6 years (range 2–14) with 73% of patients being females and 27% being males. The physical examination was unremarkable with regard to the abdomen, back,
generated, and the neurologic system in all patients. Ultrasound of
the upper urinary system was normal in 784 patients (97%) with
insignificant pyelectasis seen in 24 (3%). IVP was normal in all 19
studies. VCUG was normal in 310 patients (64.5%). Unilateral and
bilateral low grade reflux was seen in 77 and 17 patients re-
spectively. Unilateral high grade vesicoureteral reflux was seen in only
2 children. Urodynamic studies were performed in 26 patients
who did not respond to standard management. Detrusor instabil-
ity was observed in 16 patients, low bladder capacity in 5, detrusor
spincter dyssynergia in 3, poor compliance in 5, and sensory
urgency and delayed sensation in 1 patient each. One patient had
a completely normal study. Cystoscopy revealed normal findings
in 14 patients, trabeculations in 20, inflammation in 11 and 2
patients were found to have type 1 posterior urethral valves.

Conclusions: The incidence of upper tract changes and positive
anatomic findings in patients with voiding dysfunction is too low
to justify routine radiologic evaluation and cystoscopy. However,
in patients presenting with urinary tract infection, there remains
an important role for VCUG. We do not recommend the routine
use of urodynamic in patients with voiding disorders as it does
not change the management or influence the final outcome. A
good history and physical leads to the correct diagnosis and
treatment in the vast majority of children. Focus on correction of
faulty voiding behavior with judicious use of antibiotics and an-
ticholinergic therapy will lead to a favorable outcome in a vast
majority of these children.

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VASOVAGAL REACTIONS IN CHILDREN SUGGEST
AUTONOMIC DYSFUNCTION IN DYSFUNCTIONAL
ELIMINATION DISORDERS

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Horowitz, MD, FAAP and Kenneth I. Glassberg, MD, FAAP,
Brooklyn, New York. (Presented by Andrew Combs)

Introduction and Objectives: Those clinicians who study children
urodynamically in the upright position not infrequently encounter
vasovagal reactions (VVR). Because the episodes of VVR have been
so striking when they occur we wanted to determine if they
in some way were related to the voiding dysfunction itself. This
study was undertaken to evaluate the incidence and significance
of VVR.

Methods: Between 1995-98 all children undergoing videouro-
dynamic (VUDS) evaluation were monitored for VVR as evidenced
by dizziness, pallor, nausea, diaphoresis, bradycardia, hypoten-
sion or syncope. Severity of VVR was graded and timing of
reaction in relation to voiding was noted. Patients were classified
by their principal urodynamic diagnosis and the relationship with
VVR analyzed. Of 367 studies performed, 174 (81 boys, 93 girls)
with an age range of 3.5–17 yrs. met the inclusion criteria of being
studied in the upright position, nonsedated and fully verbal.

Results: VVRs were noted in 18 of 174 (10.3%) children (7 boys,
11 girls). Only one child had a previous history of VVR and none
had known neurologic disease. VVR was seen in 4 of 8 (50%)
children with bladder neck dysfunction (BND) and 9 of 33 (27.3%)
with dysfunctional voiding where pelvic floor hyperactivity
during voiding was demonstrated (PFH). BND and PFH accounted
for 13 of 18 (72.2%) of all VVRs including all episodes of syncope.
VVR occurred in 13/41 (31.7%) of children with BND/PFH but
only 5/133 (3.8%) for all other diagnostic groups combined.
(p<.0001).

Conclusions: VVR is not a rare occurrence and should be antici-
pated during upright urodynamic evaluations. It is seen predom-
nantly in the obstructive dysynergic sphincteric disorders of
BND and PFH. This association suggests a previously unappreci-
dated defect in the normal intergrated balance between the sympa-
thetic and parasympathetic branches of the autonomic nervous
system innervating the lower colon, rectum and pelvic floor, with

implications for further clinical investigation and more efficacious
treatment of these disorders.

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DEFUNCTIONALIZED BLADDERS: EFFECTS BEFORE AND
AFTER REFUNCTIONALIZATION

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Background: Defunctionalization of the bladder is seen in high
urinary tract diversion or vesicostomy in infants due to severe
ureteral or urethral obstruction and in patients with renal failure
and oligo/anuria. Despite treatment of the underlying etiology,
bladder behavior after defunctionalization is usually unpredict-
able. The aim of this study is to comparatively analyze the mor-
phological, functional and histological aspects of defunctionali-
ation and subsequent refunctionalization using a rabbit model.

Material and Methods: Fifteen young male rabbits were divided
equally into three groups. Animals in group I underwent two
successive surgical procedures: bladder division and reattach-
ment. Bladder division (BD) was performed by hemisecting the
bladder from the dome to the trigone. The right hemibladder was
left in continuity with the bladder neck and its ureter to form a
functioning chamber. The left hemibladder was completely sepa-
rated from the bladder neck and ipsilateral nephroureterectomy
was performed in order to achieve a non-functioning chamber.
Bladder reattachment (BR) was achieved by reanastomosing both
hemibladders. Group II animals received sham operations as con-
trols and group III animals were age matched normal controls.
There was a two-month interval between each successive surgery.
Serial urodynamic studies and fluoroscopic cystograms were per-
formed in all animals preoperatively, after defunctionalization in
both segments, and after refunctionalization, monthly for three
months. The rabbits were sacrificed 3 months after their last
procedure. Gross, histochemical (H&E, Masson’s Trichrome and
Sirius red) and immunocytochemical analyses (alpha-actin, colla-
gen I & III), were performed.

Results: The defunctionalized hemi-bladders in the group I
animals demonstrated lower wet weight, capacity and compli-
ance, as compared to the functional contralateral and normal
control bladders. Refunctionalization of the bladders resulted in a
progressive recovery of capacity and compliance over time, to
normal levels by three months. Histologically, defunctionalized
bladders showed an increase in connective tissue deposition in
the submucosa and between the muscular bundles. Immunocyto-
chemical studies performed with alpha-actin antibodies demon-
strated a decreased muscle fiber content. Upon refunctionaliza-
tion, the amount of muscle fiber bundles recovered to a normal
level. The defunctionalized bladders showed higher levels of type
I and III specific collagen, as compared to the contralateral blad-
ers. However, the collagen content decreased to normal levels
following refunctionalization. The sham operated control animals
(group II) showed similar results as the age matched normal
animals (group III).

Conclusion: Defunctionalization results in remarkable alter-
ations in bladder growth, capacity, compliance and distribution of
connective tissue. These findings suggest that bladder cycling is
necessary for achieving a normal bladder development and func-
tion. However, normal bladders subjected to defunctionalization
demonstrated an innate capacity to recover from these alterations
within ninety days following refunctionalization.
DIFFUSABLE GROWTH FACTORS INDUCE BLADDER SMOOTH MUSCLE DIFFERENTIATION

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Introduction: Bladder smooth muscle differentiation is dependent on the presence of bladder epithelium. Previously, we have shown that direct contact between the epithelium and bladder mesenchyme (BLM) is necessary for this interaction. In this study, we tested the hypothesis that bladder smooth muscle can be induced via diffusible growth factors.

Methods: 14 day embryonic rat bladders were separated into bladder mesenchyme (prior to smooth muscle differentiation) and epithelium by enzymatic digestion and microdissection. Five in vitro experiments were performed with either direct cellular contact or no contact: (Contact) 1) 14 day embryonic bladder mesenchyme (BLM) alone 2) 14 day embryonic bladders intact; 3) 14 day embryonic bladder mesenchyme recombined with bladder epithelium (BLE) in direct contact; (No Contact) 4) 14 day embryonic bladder mesenchyme with bladder epithelium co-cultured on the bottom of the well; and 5) 14 day embryonic bladder mesenchyme with BPH-1 (prostate cell line) epithelium co-cultured on the bottom of the well.

In each case the bladder tissue was cultured on Millicell® CM 0.4 µm membranes for 5 days in plastic wells using serum free medium. Immunohistochemical analysis of the tissue explants was performed with markers for actin for smooth muscle and pancytokeratin to detect epithelial cells.

Results:

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<th>Group</th>
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<th>3. no contact</th>
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<th>5. no contact</th>
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<tr>
<td>BLM</td>
<td>BLM</td>
<td>BLM + BLE</td>
<td>BLM + BLE</td>
<td>BLM + BPH1</td>
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<td>Growth</td>
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<td>Smooth</td>
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Conclusions: Direct contact of the epithelium with bladder mesenchyme provides the optimal environment for growth and smooth muscle differentiation. Smooth muscle growth and differentiation can also occur without direct cell to cell contact and is not specific to urothelium. This data supports the hypothesis that epithelium produces diffusible growth factors that induce bladder smooth muscle.

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CHANGING THE UROTHELIAL PHENOTYPE: ABNORMAL STROMAL-EPITHELIAL INTERACTION

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Introduction: We have previously shown that stromal-epithelial interactions are necessary for the development of the bladder. Specifically, without urothelium, embryonic bladder mesenchyme does not differentiate into smooth muscle. In this study, we tested the hypothesis that "abnormal" stromal epithelial interactions can cause phenotypic changes of the urothelium. The rational for the experimental design is to simulate the "abnormal" stromal-epithelial interactions that are created at the anastomotic site of intestinal bladder augmentations.

Methods: Tissue recombination experiments were performed by combining 14 day embryonic rat and mouse rectal mesenchyme with embryonic, newborn and adult, mouse and rat urothelium. The use of different species for the epithelium and mesenchyme confirmed cellular origin and eliminated the possibility of inadequate tissue separation and contamination. All tissue recombinants were allowed to incubate overnight and were propagated under the renal capsule of athymic host for 6 weeks. Immunohistochemical analysis was performed with uroplakins (specific for urothelium), cytokeratin 7, 14 (expressed in both urothelium and gut epithelium) and PAS (specific for mucin or goblet cells (gut epithelium)).

Results: Cellular origin was confirmed by species specific Hoechst dye 33258. The phenotype of both mouse and rat urothelium was changed to a glandular morphology under the influence of rectal mesenchyme. Immunohistochemical staining revealed a loss of the urothelial specific marker uroplakin and positive staining for mucin (PAS positive). The urothelial transformation into glandular epithelium was not a function of age occurring in the embryonic, newborn and adult urothelium.

Conclusions: "Abnormal" stromal-epithelial interactions can change the urothelial phenotype into an intestinal like epithelium. This experimental result is germane to "abnormal" stromal epithelial interactions that are created in patients with intestinal augmentations and demucosalized urothelial lined bladder patches. We propose that "abnormal" stromal epithelial interactions may play a role in the ~10 fold increase in incidence of cancer that occurs at the anastomotic site between bowel and bladder in augmentation cystoplasty.

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SURGICAL COMPLICATIONS AFTER NEPHRECTOMY FOR WILMS TUMOR: REPORT FROM THE NATIONAL WILMS TUMOR STUDY GROUP (NWTSG)

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Background: Surgical complications are a recognized morbidity of the treatment of patients (pts) with Wilms tumors. This study examines the incidence of surgical complications in the most recently completed NWTSG study.

Methods: NWTSG-4 enrolled 3,335 pts from August 1986 to August 1994. A representative random sample of 534 pts were selected from 2,290 eligible pts randomized to treatment regimens or enrolled in the followup category and treated according to NWTSG protocol. The pt records received at the NWTSG Data and Statistical Center were analyzed for surgical complications (intraoperative and postoperative).

Results: Seventy-six complications occurred in 68 pts, 12.7% of pts had at least one complication. Intestinal obstruction was the most common complication (5.1% of pts), followed by extensive hemorrhage (1.9%), wound infection and vascular injury (1.1% each). Multiple factors previously shown to be associated with an increased risk for surgical complications were analyzed by multiple logistic regression analysis. None of the previously identified risk factors such as higher local tumor stage, and intracaval involvement was associated with an increased risk of complications. Nephrectomy performed through a flank or paramedian incision was associated with increased complications (p=0.05). The risk of complications was higher if the nephrectomy was performed by a general surgeon or urologist who deals mostly with adults (RR 8.58, p=0.03, RR 3.07, p=0.08, respectively) rather than a pediatric surgeon (RR 1.0) or pediatric urologist (RR 0.66).

Conclusions: The incidence of surgical complications in NWTSG-4 was significantly lower than NWTSG-3 (12.7% vs. 19.8%, p<0.001). There has been a marked decrease in the risk of extensive intraoperative bleeding and major intraoperative complications. Factors (tumor stage, IVC involvement) previously associated with an increased risk for complications are no longer significant. This may represent
the smaller sample of pts studied in this review and that a higher percentage of high risk pts now receive preoperative chemotherapy.

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LONG TERM OUTCOME OF PATIENTS WITH BILATERAL WILMS TREATED WITH RENAL SALVAGE SURGERY
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Background: To cure children with bilateral Wilms disease and maintain adequate renal function is a surgical challenge, as successful renal salvage is technically demanding. The aim of this study was to review all patients with bilateral Wilms treated with partial nephrectomy from one institution.

Methods: This study is a retrospective review of all patients with histologically proven bilateral Wilms disease treated with a partial nephrectomy, in one institution between April 1972 and October 1997.

Results: Nineteen patients were identified, adequate follow up data was available in 18. The median age at diagnosis was 20.9 months (range 7.9–65), the median follow up was 57 months (range 12.5–297). All patients were treated with a combination of surgery and chemotherapy. Of the 36 kidneys, 8 had a nephrectomy and 22 a renal salvage procedure. Twenty patients had an in situ partial nephrectomy and 2 bench surgery with subsequent autotransplantation. The histological margins, following surgery, were clear in 19, unknown in 2 and not clear in 1. . . The renal function in these 18 patients was normal in 14, abnormal but not requiring dialysis in 2 and 2 developed renal failure. The causes of renal failure were pre-existing glomerulonephritides and a chemotherapy induced tubulopathy. Twelve of the 18 children are alive and tumour free at follow up (66%). Four children died from distant metastases and 2 from renal failure. None of the salvaged kidneys had detected local recurrence.

Conclusions: These results confirm that renal salvage procedures, in combination with chemotherapy, are a safe and effective way of treating children with bilateral Wilms disease. In addition, renal salvage surgery can maintain satisfactory renal function in the vast majority of these patients, without increasing local recurrence.

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A CONTROL RELEASE SYSTEM OF ANGIOTENIC ANTAGONISTS FOR PEDIATRIC TUMOR THERAPY
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Background: Pediatric genitourinary tumors, such as Wilms’ and rhabdomyosarcoma, are highly vascular-dependent. Angiogenesis, the process of new blood vessel formation, is a prerequisite for tumor growth and has been shown to contribute to the incidence of metastasis. The degree of neovascularization appears to be determined by the competing action of molecules that stimulate angiogenesis, such as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF), and molecules that inhibit angiogenesis, such as angiostatin and endostatin. Recently we have purified and cloned a new VEGF receptor, neuropilin-1(NP1), that is expressed by endothelial cells (EC) and by non EC such as tumor-derived cells. This receptor binds to VEGF with high affinity. We have shown that by blocking the interaction between VEGF and NP1 on EC, VEGF looses mitogenic activity. In the present study we investigated the possibility of releasing NP1 as an anti-angiogenic factor in a controlled manner using encapsulated cells.

Methods: The extracellular portion of NP1 cDNA was subcloned into an expression vector (pCDNA 3.1) that was used to transfect Chinese hamster ovary cells (CHO). CHO cells expressing the intracellular portion of NP1 (sNP1) were selected. CHO/sNP1 cells were suspended in sodium alginate solution and extruded into a CaCl2 solution were they gelled and were coated with poly-L-lysine, allowing long term release of sNP1, while isolating the sNP1 producing CHO cells (CHO/sNP1) from the host immune system. The encapsulated cells were cultured and the medium was changed every week and assayed for sNP1 using Western blot analyses. Unencapsulated cells were used as controls. Purified recombinant sNP1 was tested for inhibition of 125I-VEGF binding to EC and for inhibition of VEGF-165 induced EC proliferation.

Results: Western blot analyses performed on the media taken from the cultured encapsulated cells showed extended amounts of sNP1 when compared to non encapsulated cells. The levels of sNP1 were maintained for 1,2,3 and 4 weeks of culture. Recombinant sNP1 protein inhibited 125I-VEGF165 binding to NP1 on EC and completely repressed VEGF165-induced proliferation of EC.

Conclusion: These results indicate that extensive amounts of sNP1 are being released from the encapsulated CHO cells and that the extracellular domain of NP1 is a potent VEGF antagonist. This is the first demonstration of a system wherein transfected-specific cells are able to release anti-angiogenic factors in a controlled manner using immunoprotected encapsulation. This technique may be applicable clinically for highly vascular-dependent pediatric genitourinary tumors.

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IL-1B AND TNFA REGULATION OF INTERLEUKIN-8 (IL-8) IN HUMAN NEUROBLASTOMA TUMOR CELLS IN-VITRO

Background: Recently we have documented the expression of an important angiogenic factor, IL-8 and its receptors, in ex-vivo and in-vitro human neuroblastoma (NB) cells. Currently, little is known about the regulation of IL-8 expression by NB tumor cells. IL-1ß and TNFα are known to be important inducers of IL-8 in vivo. We hypothesized that IL-1ß and TNFα are present in NB microenvironment and that they control IL-8 expression by NB cells. To begin to address this question we performed immunohistochemical (IHC) analysis of NB specimens and in-vitro stimulation studies on cultured NB cells.

Methods: To demonstrate the presence of IL-1ß and TNFα in the tumor microenvironment archival human NB specimens (n=7) were evaluated for IL-1ß and TNFα expression by standard IHC. To determine if IL-1ß and TNFα can regulate IL-8 expression in NB we performed cell culture stimulation studies using the SK-N-MC NB cell line. Specifically, SK-N-MC cells were stimulated with 10ng/ml of IL-1ß, TNFα or control media (total n each group = 15). Supernatants were harvested at 24 and 48 hrs and evaluated for IL-8 by ELISA.

Results: IHC analysis revealed expression of IL-1ß in the tumor stroma and fibroblasts in NB. TNFα was prominently expressed in both the tumor stroma and on NB cells themselves. Stimulation studies demonstrated that both IL-1ß and TNFα significantly stimulated IL-8 production in NB cells at 24 and 48hr time points when compared to control media (see fig). Specific mean levels (±SEM) for control media at 24 and 48hrs were: 26.23 pg/ml [±0.88] and 38.31pg/ml [± 3.14]. IL-1ß stim. levels at 24 and 48 hrs were 107.97 pg/ml [±31.01] and 348.93 pg/ml [±61.40]. TNFα stim. levels at 24 and 48hrs were 198.48 pg/ml [±18.22] and 411.42 [±23.22].
Conclusions: Our studies demonstrate that IL-1β, TNFαs and IL-8 are all present in the NB tumor microenvironment. Additionally we have shown IL-1β and TNFα upregulate IL-8 expression in cultured NB tumor cells. As IL-1β and TNFα appear to be present in the NB microenvironment they may contribute to the in-vivo regulation of IL-8 in NB. Understanding the regulatory cascade promoting angiogenesis in NB may lead to the development of effective anti-angiogenic therapy.

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FUNCTIONAL AND STRUCTURAL CHANGES IN GUINEA PIG BLADDER UPON URETHRAL OBSTRUCTION


Background: Urethral obstruction induces changes in several parameters for bladder function and structure. The individual response to urethral obstruction is at present unpredictable. We studied changes in bladder contractility, compliance, collagen composition and three dimensional matrix structure. The time sequence along which these changes occur is not known. We have developed a guinea pig model for urethral obstruction where bladder function is measured repetitively in individual animals. We have used this model to document the longitudinal changes in bladder contractility and compliance and relate these to bladder collagen composition and 3-D structure.

Methods: In 34 immature male albino guinea pigs a silver jeweller’s jump ring placed loosely around the urethra induced urethral obstruction. Four animals were sham-operated, 2 served as controls. Before and 1 to 11 weeks after ring-removal, pressure-flow studies were done weekly from which we have calculated the compliance, c (ΔV/Δp) and bladder contractility, Wmax (power per bladder surface area). At the end point bladder material was obtained and analyzed for collagen type I, III and IV- mRNA expression and protein expression. Bladder samples were also made cell-free and analysed by SEM.

Results: Urethral resistance rapidly and consistently rose. Contractility first increased then decreased. Compliance continuously decreased. Bladder weight increased from 0.5g to 3.0–4.9g in weeks 5–12. In the basal urothelium the mRNA signal for collagen-I and -III (weaker) increased the 1st week, maximal in the longest obstructed animals and correlated to decreasing compliance. Increased collagen deposition beneath the urothelium was confirmed with immunohistology. ASEM analysis of cell-free matrix showed loss of collagen organization.

Conclusion: In the first weeks of obstruction the Guinea pig bladder adapted by increasing contractility and decreasing compliance. After prolonged obstruction, contractility decreased. Compliance continued to decrease after contractility reached its peak. While the first decrease in compliance may be due to increased muscle tone, the latter most likely is due to matrix-collagen deposition as reflected by the mRNA and antibody data. Possibly the loss of collagen organization also plays a role.

In future studies we will use our animal model to study if the observed changes can reverse after removal of the obstruction.
studies in our laboratory have demonstrated that mechanical stretch induces Heparin-binding epidermal growth factor-like growth factor (HB-EGF) expression in cultured bladder smooth muscle cells, mediated by an autocrine release of Angiotensin II (Ang II). HB-EGF is produced in the smooth muscle of the bladder and stimulates smooth muscle proliferation. The peptide hormone Ang II has been implicated in hypertrophic responses in smooth muscle cells when it binds and activates angiotensin type 1 (AT1) receptors. In this study, in order to simulate an in vivo model, whole bladder muscle strips were exposed to passive and active tension utilizing electrical field stimulation (EFS) and HB-EGF expression was measured. We also evaluated whether the stretch induced HB-EGF expression was Ang II dependent.

**Methods:** Rats were anesthetized and their bladders were removed. The bladder base was separated from the bladder body which was cut into strips, placed into a tissue bath containing Krebs solution at 37°C, and bubbled with 5% CO2 and 95% O2. One end of the strip was attached to a fixed hook and the other to a force transducer. Force measurements were displayed on a strip chart recorder. Smooth muscle strips were placed under 2 grams of tension and allowed to equilibrate for 45–60 minutes. Platinum electrodes were arranged on both sides of the muscle strips for EFS using square wave pulses of 20 volts, 0.4 Hz, and 5 milliseconds duration. Muscle strips were subjected to passive or active tension for 4, 6, and 8 hours. Muscle strips were also exposed to losartan, an AT1 receptor inhibitor to determine if HB-EGF expression was Ang II dependent. Finally, the strips were frozen in liquid nitrogen and relative levels of HB-EGF mRNA were measured by semi-quantitative RT-PCR.

**Results:** 1) Passive stretch of smooth muscle strips resulted in an increase in HB-EGF mRNA expression in a time dependent fashion. 2) Electrical field stimulated contraction of the muscle strips augmented the increase in HB-EGF mRNA expression. 3) AT1 receptor inhibition blocked the contractile activity induction of HB-EGF expression.

**Conclusions:** In obstructed bladders, hypertrophy of the smooth muscle cells results in alterations in physiologic properties and failure of the bladder to store urine or empty properly. This growth induction may result from repetitive mechanical stresses experienced by the bladder smooth muscle cells as a result of obstruction. Active increases in bladder wall tension through contraction can regulate HB-EGF gene expression, which as a potent mitogen, can mediate cell growth in bladder muscle and result in bladder hypertrophy. HB-EGF expression induced by contractile activity is in part due to autocrine Ang II activity. These findings suggest a potential pharmacologic role for losartan in blocking bladder smooth muscle hypertrophy.

**37 INCREASED SUSCEPTIBILITY TO AND EVIDENCE OF FREE RADICAL MEDIATED MEMBRANE TOXICITY AFTER BLADDER OUTLET OBSTRUCTION**

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**Background:** While mechanical stretch is responsible for many of the bladder wall muscle changes after outlet obstruction, growing evidence supports a role for abnormalities in bladder wall perfusion. In this study we report evidence of free radical mediated toxicity to the membrane proteins by nitrotyrosines (products of a reaction between superoxide, nitric oxide and the tyrosine residues in proteins) and changes in the cell’s ability to resist such oxidant stress.

**Methods:** Standardized outlet obstruction were created in adult New Zealand White rabbits; muscle strip studies categorized the bladders as compensated (force >50% of control) or decompensated (force < 50% of control). From muscle tissue stored at -80°C, a microsomal membrane and cytosolic fraction were prepared. Three groups were studied: control, compensated, and decompensated. Equal amounts of membrane protein were transferred to nitrocellulose filters and a dot blot analysis was performed using a primary monoclonal antibody specific to the nitrotyrosines, a 2nd antibody and a chemiluminescence detection system. Equal amounts of cytosolic protein were assayed for free radical scavenging ability by competing for cytochrome C reduction in the presence of a xanthine/xanthine oxidase free radical generating system.

**Results:** Nitrotyrosine expression by dot blot analysis and normalized to controls by scanning densitometry was increased by 1.1 and 2.2 in the compensated and decompensated groups respectively. Free radical scavenging ability (expressed as % of control) was determined for the same 3 groups: control 100%, compensated 94% ±7% (p=ns vs control), decompensated 37% ±10% (P<0.05 vs control).

**Conclusion:** This data offers direct evidence for free radical mediated damage to the smooth muscle membranes and also suggests that with bladder decompensation, there is a loss of the smooth muscle cell’s ability to scavenge free radicals. Loss of membrane proteins such as calcium ion pumps may, if left unchecked, trigger apoptosis. The clinical significance of these findings is that they suggest a medical approach to lessening the effects bladder outlet obstruction by free radical scavenging drugs.

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**38 MECHANICAL SIGNALS ACTIVATE DIVERSE MEMBRANE RECEPTORS INVOLVED IN GROWTH FACTOR SYNTHESIS IN BLADDER SMOOTH MUSCLE CELLS**

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**Introduction:** The cellular mechanisms that regulate bladder smooth muscle cell (SMC) growth in response to mechanical forces remain to be defined. Heparin-binding epidermal growth factor-like growth factor (HB-EGF) is synthesized by bladder SMC and is a potent autocrine mitogen. Because of its biological activity and site of synthesis, HB-EGF may be an important growth factor involved in the bladder’s response to urethral obstruction. Previous studies from our laboratory have determined that mechanical stretch induces HB-EGF expression in SMC and that stretch-activated HB-EGF expression is mediated by the autocrine release of angiotensin II (Ang II) and is dependent on a functional AP-1/Ets site within its promoter region. In this study, we sought to further define the intracellular signaling mechanisms involved in stretch-activated induction of HB-EGF expression in rat bladder SMC.

**Methods:** Rat SMC were established in culture according to our previously published methods. Cells were grown on collagen coated, silicon elastomer-bottomed culture plates and subjected to either continuous cycles of stretch/relaxation or direct stimulation with Ang II in the presence and absence of specific inhibitors (AT1 receptor, ErbB1, ErbB2, p38 MAPK and p44/42 MAPK). Cells were harvested at various time points (10 min. to 24 h) following stimulation. Relative levels of HB-EGF mRNA were measured by semi-quantitative RT-PCR. Western blot analysis of specific phosphorylated proteins (p38, p44/42 MAPK, JNK/SAPK) was used to identify activated intracellular molecules involved in the signal transduction of mechanical stretch. Additional evidence for the involvement of specific signal transduction pathways was provided by transfection experiments with pathway-specific activator fusion proteins.
Western blot analysis and electrophoretic mobility shift assays were used to identify specific transcription factors (e.g., Stat1, Stat3 and Ets proteins) involved in stretch-activated induction of HB-EGF expression.

**Results:** Stretch-induced increases in HB-EGF mRNA levels were dependent on signaling through AT1 and ErbB2 receptor-dependent pathways, based on experiments with specific pharmacologic inhibitors of AT1 and ErbB2 receptors. Stretch-induced increases in SMC growth were partially dependent on signaling through AT1 receptors and completely dependent on signaling through ErbB2 receptors. Pharmacologic inhibition, western blot and fusion protein reporter experiments indicate that both receptor systems activate p38 and JNK mitogen activated protein kinase cascades which converge on a cognate AP-1/Ets site in the HB-EGF promoter. We previously identified this AP-1/Ets site as a stretch-responsive element in bladder SMC.

**Conclusions:** These data have delineated, for the first time, a signaling pathway in bladder SMC which is activatable by mechanical forces and which mediates expression of a potent growth factor implicated in bladder outlet obstruction. These data are consistent with a role for HB-EGF as an important molecular mediator of bladder hypertrophy. Pharmacologic manipulation of AT1, ErbB2 receptors and HB-EGF is possible in vivo and may provide a novel means of treating obstructive bladder disease.

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**NEONATAL UTERINE HYPERTROPHY AS A CAUSE FOR TEMPORARY BLADDER OUTLET OBSTRUCTION IN INFANT GIRLS**

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**Introduction:** Maternal hormones are responsible for several well-recognized signs in the normal female neonate such as labial hypertrophy, florid vaginalis and sometimes even spotting of blood from the uterine endometrium. A physiological hypertrophy of the uterine cervix also exists in the perinatal weeks of female neonates as a result of this hormonal stimulation. The diameter of the cervix ranges between 1.3 cm at 34 weeks and 2.4 cm at term in normal, healthy newborn females. Cervix diameter drops down to a diameter of approx. 0.5 to 0.8 cm at 3 months of life and remains that size until puberty begins. In the neonatal female, ultrasonography of the uterine cervix shows an impressive size, compared to the bladder, and sometimes, the cervix can be seen to elevate the bladder neck.

**Patients and Methods:** Between 1985 and 1996, 16 healthy female neonates have presented in our department with unexplained failure to empty their bladder immediately after birth. Gestational age ranged from 34 to 41 weeks. Except for a mild dilatation of the upper tract in 4 cases and a significant dilatation in one case, no upper tract complications were seen. In the first 3 cases, a neurogenic bladder was excluded by Plain X-ray of the spine, ultrasound of the myelum and urodynamic study. In the cases with upper tract dilatation, vesico-ureteral reflux was excluded by VCUG. The common factor in all patients is a relatively large uterine cervix that compresses the bladder neck against the symphysis, combined with a large bladder with incomplete emptying. Symptoms of difficult bladder emptying subsided a few days after birth in all patients. Two patients needed an indwelling catheter for a few days and resumed voiding after catheter removal. Upper tract dilatation subsided in the first few months of life. With a follow-up of several years no long-term complications have been seen.

**Conclusion:** Neonatal hypertrophy of the uterine cervix can cause a temporary bladder outlet obstruction that, at first, can mimic a neurogenic bladder. Once the anomaly has been recognized, a wait and see policy will generally show relief of symptoms within a few days. Rarely, an indwelling catheter is needed for a few days. The question arises whether this phenomenon is responsible for part of the upper tract dilatation, seen prenatally, that subsides rapidly after birth.

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**DOES NEONATAL PYELO-URETEROSTOMY WORSEN BLADDER FUNCTION IN CHILDREN WITH POSTERIOR URETHRAL VALVES?**

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Recently, some authors have suggested that the dysfunction present in the bladders of some children with PUV is more frequent and severe in those whose bladders were defunctionalized in their first months of life by vescicostomy or pyelostomy when they did not respond well to valve ablation.

**Goal:** To determine whether long-term bladder dysfunction is more frequent in children who undergo early supra-vesical urinary diversion (bilateral pyelo -ureterostomy) than in those who undergo valve ablation.

**Material and Method:** Urodynamic studies were performed in 59 boys with severe PUV divided into two groups based on initial treatment: A) Valve ablation (30 p.) B) Neonatal cutaneous pyelo-ureterostomy (29 p). Average period of diversion was 13 months. All patients had at least 2 urodynamic studies during the followup to diagnose their bladder dysfunction (X = 2.4) and mean patient age at the latest urodynamic study was similar in both groups.

**Results:** Of the 59 boys, 25 (42%) had over-distended or normally behaving bladders and 34, (58%) had some bladder dysfunction (instability 37%, poor compliance 15%, and myogenic failure 5%). In the group A (patients with ablated valves, 30 p.), 14 p. (46.6%) had normally behaving bladders and 16 p. (53.4%) had some kind of dysfunction. Of the 29 patients (Group B) treated with pyelo-ureterostomy, 11 (38%) had normally behaving bladders and the other 18 (62%) had some type of dysfunction. Analysis of the bladder dysfunctions found in our patients together with initial treatment (valve ablation or pyelo-ureterostomy) showed that the two types of treatment were associated with the same types of bladder dysfunctions and in similar proportions.

**Conclusions:** Therefore neonatal supra-vesical urinary diversion has no adverse effects on their posterior bladder function and poor bladder function is probably due to some damage to the detrusor muscle as a consequence of intrauterine infravesical obstruction.

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**IMPROVED BLADDER EMPTYING IN POSTERIOR URETHRAL VALVE PATIENTS AFTER SELECTIVE ALPHA BLOCKER THERAPY.**

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**Background:** Interest in bladder malfunction in children with posterior urethral valves has focused mostly upon early life when the bladder is most affected by high pressures due to outlet obstruction. As boys with valves grow older, problems with bladder function may persist and continue to cause hydroureter, UTI, and incontinence. These boys often fail to store and empty urine at acceptable pressures and they often cannot empty completely. The purpose of our study was to investigate potential benefits of selective alpha blocker therapy to improve bladder emptying in PUV patients.

**Methods:** Five patients with a history of PUV ranging from 3-9 years old (mean 5.6 y.o.) were identified to have poor bladder emptying. Poor bladder emptying was documented by post void residual (PVR) measurements, symptomatology, as well as by
demonstration of new hydronephrosis on ultrasound. All patients were initially placed on 0.5 mg of doxazosin nightly and followed monthly with PVR measurements and ultrasonography. Maximum urinary flow rates were also measured in those patients able to void.

Results: New or increased hydronephrosis was seen in 3 patients (2 bilateral, 1 solitary kidney) while chronic hydronephrosis was present in the remaining 2 patients (1 solitary kidney). After alpha blocker therapy, hydronephrosis resolved in 2 patients improved in 2 patients, and remained unchanged in 1 patient. Bladder emptying was also noted to markedly improved in 4 patients after alpha blocker therapy with a 72% mean reduction in PVR (range 35–96%). Three patients had pre- and post-treatment peak flow rates for comparison and demonstrated an average 5-fold increase in their maximum flow rate. Two patients were unable to void prior to therapy. Only one patient with a previous ureteral bladder augmentation demonstrated a persistent large PVR (6.5% reduction) despite improved flow on uroflowmetry (10-fold increase).

Conclusions: In our early experience, patients with valve bladders particularly appear to benefit from selective alpha blocker therapy. Not only is bladder emptying improved, but hydronephrosis due to elevated bladder pressures has substantially improved in most patients. Future investigation is necessary to determine if selective alpha blocker therapy may provide long term benefit in patients with PUV.

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THE NEWBORN EXSTROPHY BLADDER TOO SMALL FOR PRIMARY CLOSURE: EVALUATION, MANAGEMENT AND OUTCOME.

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Background: The surgical approach to the small newborn exstrophyed bladder remains undetermined. Various approaches to long term management of these children have been implemented. The authors investigated their experience in late primary closure of the small exstrophyed bladder template.

Methods: The charts of 605 patients treated and followed for the exstrophy-epispadias complex were reviewed. Fifty of these underwent primary closure (either at our institution or elsewhere) after the age of six months. Twenty of these patients had a bladder template which was judged too small to close in the newborn period. The other 30 patients had delayed closure for a variety of financial, geographic, other circumstantial or unknown reasons.

Results: Of the 20 children who had delayed closure due to a small bladder template there were 18 males and 2 females. Follow-up time ranged from 1–32 years (mean 21 years). Primary closure was performed at a mean age of 1.2 years (range 6mo-2yrs). Osteotomies were performed in 17. Nine of 20 patients achieved continence after gaining sufficient bladder capacity for bladder neck reconstruction. Five of 20 patients required enterocystoplasty to augment bladder volume, and perform clean intermittent catheterization (2 per stoma, and 3 per urethra). One patient required a colon conduit for very small bladder and one a cystectomy and ureterosigmoidostomy due to rhabdomyosarcoma. Four patients are incontinent, 2 of these are awaiting bladder neck reconstruction, and 2 had a failed bladder neck reconstruction.

Conclusion: Delayed primary closure of a small exstrophyed bladder template permits the native bladder tissue time to grow to a size that is feasible for successful closure in most patients. An epispadias repair can usually be performed at the same time especially with testosterone stimulation. Bladder neck reconstructive techniques have achieved continence without the need for augmentation or bladder replacement in 45% of patients. Even in patients who do not achieve adequate capacity for bladder neck reconstruction, preservation of the native bladder template allows for easier future augmentation and ureteral reimplantation.

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PERI-URETHRAL MUSCULAR COMPLEX IDENTIFICATION AND REASSEMBLY IN EXSTROPHY-EPISPADIAS REPAIR: RATIONALE AND TECHNIQUE

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Background: Achievement of continence is one of the main goals of reconstruction in exstrophy-epispadias complex (EEC). It has been postulated that all the normal components of the lower genito-urinary tract are present in the EEC, albeit they are displaced laterally and incompletely developed. The total disassembly technique for epispadias restores normal anatomical relationship of the male external genitalia components, with good cosmetic and functional results. Its extension to the complete primary repair of exstrophy allows deeper positioning of the bladder neck and posterior urethra within the pelvic diaphragm. Nevertheless, poor attention has been devoted so far in identifying and repositioning the urethral sphincteric mechanism. We consider the identification of the urethral striated sphincteric complex by bipolar electric stimulator and its appropriate reassembly as a main step in the repair of EEC.

Methods: Nine consecutive patients (7 males and 2 females), 1 to 9 years old had bladder and urethrogenital repair during the last 4 years: three of them had EEC complete repair in one time (1 male newborn and 2 females), 4 were exstrophies previously closed and 2 boys had incontinent epispadias. In the male EEC patients, after bladder plate closure, mobilization of the urethral wedge and glans with splitting of corporeal bodies is performed. Accurate dissection is carried out on each side of the bladder neck and posterior urethra, laterally to the prostatic tissue which must stay joined with the proximal urethral wedge as one unit. A vertical midline incision is performed posteriorly and extended to the perineal body looking for the anterior pelvic floor musculature (which is displaced laterally), and the anorectal sphincter complex (which lies posteriorly). The use of bipolar electric stimulator is essential in order to detect the muscular fibers of the pelvic diaphragm and mobilize them around the tubularized urethral wedge at the level of the prostatic tissue. The bulbocavernosa are reapproximated along the midline over the posterior urethra, completing the reassembly of anterior pelvic floor musculature. In the 2 female patients both the urethral plate and the vagina are mobilized posteriorly through the midline dissection of the perineal body. Looking for the delicate muscular fibers of the pelvic floor which normally surround the female urogenital complex. No attempt is made in this phase to perform any bladder neck plasty or antireflux surgery, in order not to interfere with the lower tract functional maturation.

Results: At 4 to 42 months of follow-up all patients revealed good cosmetic appearance. Cyclic micturition with urinary stream and dry intervals of 30 to 90 minutes were observed in 7 out of 9 patients (77.7%), whereas the remaining 2 patients still present continuous dribbling. No significant upper tract dilatation has been observed, but febrile tract urinary infection occurred in 4 patients, despite all being on antibiotic chemoprophylaxis. One year after surgery, a cystogram under anesthesia was performed. Bladder capacity ranged from 35 cc to 80 cc. Grade 1 to 4
reflux was present in all patients. A meatal and distal urethral stricture occurred in one male exstrophy newborn, who required surgical meotomy and re-do glansplasty. No urethral fistulas were observed.

Conclusion: Early restoration of bladder-urethral physiologic balance in a coordinated activity is feasible for a progressive achievement of voluntary micturition control in EEC patients. Careful division of the anterior aspect of the perineal membrane and midline reassembly of the pelvic diaphragm muscles is completed by the surgical reconfiguration of the urethral sphincteric complex around the posterior urethra. We believe that urethral sphincteric mechanism behaves similarly to the muscular complex in anorectal malformations from the embryological, anatomical and functional standpoint. The correct reconfiguration of the pelvic anatomy in a normal fashion on the midline is the key for the achievement of voluntary continence. Therefore, neither trigone surgery nor bladder neck plasty is performed at this stage, to avoid any damage to the neuromuscular maturation of the trigone and bladder basement during the initial steps of the lower tract functional development. The accurate identification of the striated sphincteric structures, utilizing the bipolar stimulator and its re-assembly around the posterior urethra could allow for better results in terms of restoration of normal bladder function in a coordinated fashion, looking for voluntary urinary continence in EEC patients.

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PRELIMINARY EXPERIENCE WITH NEONATAL COMPLETE PRIMARY CLOSURE OF EXSTROPHY/EPISPADIAS

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Background: Over the past 20 years, a staged approach to the management of exstrophy/epispadias complex has been used in most pediatric centers. Using this approach, the bladder remains defunctionalized in early childhood and appropriate bladder capacity is often not achieved. Complete primary closure potentially allows early bladder cycling and bladder expansion, and may eliminate many long-term reconstructive concerns. Historically, single stage closure has been associated with upper tract decompensation and bladder deterioration. This report deals with short term outcomes using complete primary repair.

Methods: Between November 1995 and October 1998, 6 newborns (4 male and 2 female) had a single stage repair of exstrophy/epispadias. Five repairs were performed in the first 24 hours of life and pelvic osteotomies were not performed. The other repair was completed at 3 months of age in conjunction with anterior iliococcygeus osteotomies. No attempt was made to perform a bladder neck reconstruction. Mermaid traction or a spica cast was used for immobilization and all infants were discharged from the hospital within 7 days. Ureteral stents and the urethral catheter were removed two weeks after surgery and the suprapubic tube was removed four weeks after surgery. The infants have been maintained on prophylactic antibiotics for reflux. Ultrasound scans were obtained every 6 months and bladder capacity was determined using voiding cystourethrography.

Results: All primary closures were successful. The average follow-up is 22 months. One male had a foreshortened urethra and primary closure resulted in a penoscrotal hypospadias that was corrected with an island flap at 6 months of age. One male had a urethrococcygeal fistula that was closed at 6 months of age. All had a dry interval and began voiding when the suprapubic tube was removed. The five oldest children had a VCUG and bladder volumes range from 60 to 150cc (mean 95cc). No child has developed hydronephrosis. Three children had febrile urinary tract infections (UTI’s). One female with recurrent UTI’s had a bilateral ureteral reimplant at 25 months of age. Two males with febrile UTI’s have no evidence of urethral obstruction and unilateral grade III reflux and are being maintained on preventive antibiotics.

Conclusions: Primary complete closure of exstrophy/epispadias can be performed with minimal morbidity. There is no short term evidence of upper tract deterioration or bladder dysfunction. Bladder refunctionalization may increase the risk of febrile UTI. Long-term follow-up is required to know whether this technique will result in a decreased need for bladder neck reconstruction and bladder augmentation in exstrophy patients.

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MANAGEMENT OF FEMALE BLADDER EXSTROPHY/EPISPADIAS WITH TOTAL UROGENITAL COMPLEX MOBILIZATION

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Background: Female bladder exstrophy/epispadias has traditionally been approached in a staged fashion. However, there is a paucity of literature regarding the subsequent management of the short and anteriorly displaced urethra, the anteriorly positioned and often stenotic vagina, bifid clitoris, and laterally divergent mons pubis. In addition, the lack of ligamentous attachments to the female internal organs results in a high incidence of vaginal and uterine prolapse post adolescence that requires surgical correction. Herein, we present our current management of the newborn and older female exstrophy/epispadias patient with the technique of total urogenital complex mobilization that addresses the above concerns.

Methods: Since 1997, a total of 6 female patients with variants of the exstrophy/epispadias complex have undergone surgical repair utilizing total urogenital complex mobilization. Three patients (1 newborn and 2 school age) had classic bladder exstrophy, two school age patients had cloacal exstrophy, and one school age patient had primary epispadias. Total urogenital complex mobilization involved treatment of the urethra and vagina as a single unit. Complete disassembly of the pelvic diaphragm/floor that is anterior to the rectum was required in order to reposition the urethra and vagina to their proper anatomical position in the perineum. The pelvic diaphragm was then reconstructed anterior to the urogenital complex to recapitulate the normal female pelvic floor anatomy. Patients without bladder neck ligation did not undergo a formal bladder neck procedure such as a Young Dees repair. Uterine suspension with prolene mesh was simultaneously performed in one patient to prevent future uterine/vaginal prolapse. Additional urological procedures in these patients included bladder neck closure (3), enterocystoplasty (3), and creation of a catheterizable stoma (3). Monsplasty was performed in all patients.

Results: All patients have an anatomically correct position of their urogenital complex. All of the vaginas reached the perineum without the need for skin flaps. All patients have adequate vaginal caliber without evidence of stenosis. The two patients (newborn classic bladder exstrophy and primary epispadias) that did not have a formal bladder neck procedure are currently having dry periods with normal bladder contractions. The 3 patients that had bladder neck closure and augmentation are dry on intermittent catheterization every 4 hrs. The one patient that was previous diverted with a ureterosigmoidostomy has maintained her rectal continence.

Conclusions: The female with exstrophy/epispadias has unique anatomic defects in the urogenital complex that require special attention. The anterior displacement of the bladder, urethra, and vagina with the concomitant lack of development of the anterior pelvic floor musculature make a single stage total urogenital complex mobilization repair ideal in this population. The preliminary
results utilizing this technique have been functionally and cosmetically pleasing. Whether repositioning of the urogenital complex into the normal anatomic position will improve bladder dysfunction, urinary continence rates and decrease or eliminate the need for future surgery will only be known after further long term follow has been completed.

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BLADDER MATRIX CHANGES IN EXSTROPHY-EPISPADIAS COMPLEX. DEVELOPMENTAL DEFECT OR ACQUIRED IN UTERO?

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Background: It has been shown previously that the matrix composition of the bladder wall in human exstrophy-epispadias complex is overthrowned, with predominance of connective tissue and collagen, and poorly represented muscular component. Aim of this study was to reproduce these changes in two different models of bladder exstrophy, i.e. with short and long gestational age (GA), and see whether the resulting fibrosis is mainly the result of lack of development or it is secondary to other phenomena.

Methods: Bladder exstrophy was reproduced in 6 fetal lambs and in 30 fetal rabbits. Sheep were operated on at 75 ± 5 days of GA (term = 140 days), and rabbits at 24 ± 1 days of GA (term = 31 days). Under general halothane anesthesia, the uterus is exposed and a small hysterotomy carried out. The hind end of the fetus is exposed, the fetus’ abdomen is entered and the bladder identified, opened on the midline, and sutured to the skin after removal of two triangular wedges of abdominal wall. The fetus is then returned to the uterus and pregnancy is allowed to proceed. Fetuses are retrieved near term by cesarean section (135 days in the sheep and 29 or 30 days in the rabbits). Alive newborn animals are weighted and sacrificed. The bladder is excised, washed, weighted and fixed in 7% buffered formalin. Specimen are then embedded in paraffin and cut in 2 to 6 μ sections. Part of these are stained with the Masson trichrome method for computerized morphometry as previously reported, and areas of smooth muscle and connective tissue are quantitatively measured. The rest are used for the immunoassay of Actin, type I Collagen and Vimentin (Sigma-Aldrich, Milan, Italy) Specimen are incubated for 30 minutes with the antibody diluted in 1% PBS-BSA solution. To reveal the complexes we use the Streptavidin Peroxidase method. The same steps are undertaken on the bladders of 6 control lambs and 20 control rabbits.

Results: All lambs and 21 rabbits (70%) survived. The manipulation reproduc the complete extrophic vesical plaque in all 6 lambs and in 20 rabbits (1 resulted in a vesicostomy). Morphometry (median values) revealed that connective tissue was 65% in the exstrophy rabbits (45% in controls) and 70% in exstrophy lambs (29% in controls). Smooth muscle was 35% in exstrophy rabbits (55% in controls) and 30% in exstrophy lambs (71% in controls). Actin was present in 62% of control rabbits and in 100% of control lambs and only in 27% and 25% of experimental specimens respectively. Vimentin was present in the exstrophy groups (85% of rabbit and 100% of lamb specimens) and was absent in the controls of both animals. Type I Collagen was present in all sheep specimens but positivity was stronger in the exstrophy group. In the rabbit, 83% of controls were moderately positive, whereas 100% of the exstrophies were positive with half of these showing high degree of positivity.

Conclusions: These data indicate that the relative changes of the two main components of the bladder matrix, which take place in the exstrophy-epispadias complex, can be reproduced in different animal models. The lack of actin expression in the exstrophic bladders probably reflects the fact that these bladders are defunctionalized in utero, and can be clearly seen in both the long and short GA models. Also, the high expression of vimentin is secondary to the differentiation of the mesenchymal cells into fibroblasts precursors and fibroblasts instead of myoblasts and myocytes, reflecting a tendency to deviate from muscle development to collagen production. This phenomenon is present in both the experimental lines, indicating that the real cause is developmental. However, the same is more evident in the long GA model, probably because the time of exposure to the amniotic fluid plays an additional role in the process of fibrosis.

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CLINICAL AND BIOMECHANICAL ANALYSIS OF HIPS IN ADULTS WITH BLADDER EXSTROPHY

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Background: We analyzed shape and stress on the hip joint in exstrophy and reviewed the status of hips in adults with uncorrected exstrophy.

Methods: Fourteen patients aged 16 to 52 years born with classic bladder exstrophy were studied. Patients were matched for age and gender with 14 controls. AP pelvis radiographs were used for biomechanical analysis based on the single-stance phase of gait. Joint force and joint stress (force/area) were calculated relative to partial body weight by the method of Legal (1987). Clinical assessment was by Iowa hip score and radiographic grading. Statistical analysis was done using t tests.

Results: For the exstrophy patients, the mean relative joint force was significantly higher than control (4.2 ± 0.91; 3.0 ± 0.3) (p<0.01). The mean relative joint stress for exstrophy patients was significantly higher as well (p<0.05). The increase in force and stress appeared to be due to three factors: (1) the mean distance from the body center to the center of the femoral head was significantly increased (p<0.001) in bladder exstrophy (12.35 ± 1.05 cm) versus controls (10.31 ± 0.70 cm) (approximately 30% increased). (2) The mean distance from the greater trochanter to the femoral head center (I) was significantly less (p<0.02) for exstrophy patients (5.2 ± 1.2 cm) compared to controls (6.5 ± 0.8 cm). (3) The center-edge angle (CO angle) was significantly decreased in exstrophy patients (25.0 ± 9 deg.) Versus control (33 ± 7 deg) (p<0.05). Two of the adults with exstrophy had decreased Iowa hip scores and radiographic evidence of arthrosis.

Conclusions: The force and stress on the hip joint are increased in adult bladder exstrophy patients. Increased joint load and stress can lead to an earlier onset of DJD. These results need corroboration by larger series. It remains to be seen whether closing the pelvic ring at exstrophy closure may help reduce these factors and affect the outcome of the hip.

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DETERMINATES OF CONTINENCE AFTER BLADDER NECK RECONSTRUCTION IN THE BLADDER EXSTROPHY POPULATION

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Background: Continence in the bladder exstrophy population requires the coordinated and staged surgical management involving the successful closure of the exstrophy bladder, early epispadias repair, and bladder neck reconstruction (BNR) after an appropriate bladder capacity. In some select cases, initial bladder closure and epispadias may be closed concomitantly. To further delineate factors that may predict eventual continence after bladder neck plasty, we have retrospectively reviewed our patient records.
Methods: The records of 88 patients who underwent total bladder extrophy reconstruction at our institution between 1975 and 1997 were reviewed. 57 patients with BNR were available for analysis after excluding 23 patients awaiting BNR, 3 patients who achieved continence without BNR, 4 patients with recent BNR, but less than one year follow-up, and 1 patient lost to follow-up. Their medical records were reviewed and data analyzed.

Results: The median and mean age for primary closure were 10 days and five months, respectively. The average age of BNR was 4.4 years with a mean capacity of 88 cc. Of these 57 patients, 42 (74%) are continent and voiding urethrally without need for augmentation or CIC. 9 (16%) patients have social continence, dry for more than three hours during the day, 2 patients required diversion for continence after failed BNR. 3 patients are wet. Analysis of bladder capacity measurements prior to BNR revealed patients with bladder capacity greater than 75 cc at the time of BNR or with an average increase in capacity of more than 21 cc/year resulted in better outcome. Whereas 2 patients were wet and 2 required urinary diversion in the group with the smaller bladder capacity and poor bladder growth, only one patient was completely wet in the optimal group. No correlation between age of BNR and continence was found.

Conclusion: Determinates of continence in the bladder extrophy population are multifactorial. In our experience 74% are all completely dry, day and night, and 89% can obtain "social continence," being dry for at least 3 hours. However, with careful evaluation of bladder capacity and bladder growth, urinary continence may be improved in this population with better patient selection.

THE MODIFIED CANTWELL-RANSLEY REPAIR IN EXSTROPHY AND EPISPADIAS: TEN YEAR EXPERIENCE

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Background: In the exstrophy-epispadias population, male adolescents consider the oddly appearing genitalia, with a short widened penis, to be a greater psychosocial problem than incontinence and therefore every effort should be made to restore the penis to a normal status. Therefore the authors evaluated their ten year experience with the modified Cantwell-Ransley epispadias repair technique to determine the complications and long term results.

Methods: A retrospective chart review was performed on 605 exstrophy-epispadias data-base patients. 93 males (79 with classic bladder extrophy and 14 with complete epispadias) underwent a modified Cantwell-Ransley epispadias repair over the last ten years. Primary repair was performed in 77 boys (65 with classic bladder extrophy and 12 with epispadias), and secondary repair was performed after prior failed reconstruction in 16 boys (14 classic epispadias and 2 with complete epispadias). Epispadias repair was combined with relosure of bladder extrophy in 10 patients.

Results: At a mean follow up of 68 months (4–120mo), 87 patients had a horizontal or downward angled penis while standing and 88 patients pass urine per urethra. Fistulas developed in 22 patients (23%). In 4 patients the fistulas closed spontaneously within the first 3 months after surgery and 18 patients (19%) underwent a separate procedure to close the urethrocutaneous fistula. Seven patients developed a urethral stricture at the proximal anastomotic area and 5 patients had minor skin separations (4 exstrophy, 1 epispadias) of the dorsal penile skin closure. Catheterization or cystoscopy in 77 children revealed an easily negotiable neourethral channel.

Conclusion: The authors conclude from their ten year follow-up that the single stage modified Cantwell-Ransley epispadias repair technique creates a cosmetically satisfactory penis and produces a straight, catheterizable neourethral channel with an acceptable complication rate. However, definitive assessment of genital reconstruction must be deferred until all of these boys are sexually mature and active. While many methods of epispadias repair exist, meticulous follow-up of the urethra, patient selection and surgical experience remain the milestones for success.

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Tc-99m DMSA RENAL SCAN ABNORMALITIES IN INFANTS WITH STERILE, HIGH GRADE VESICOURETERAL REFUX

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Introduction: Although vesicoureteral reflux (VUR) associated with bacteriuria may cause renal scarring, sterile VUR is thought not to cause renal injury. However, in many infants with high grade reflux, renal scarring is found even though bacteriuria is not present. In this study, we sought to determine the incidence of renal abnormality as assessed by DMSA renal scan in infants with high grade VUR but without a prior history of urinary tract infection.

Methods: We retrospectively reviewed the results of Tc-99m DMSA renal scan performed during the first six months of life on infants with VUR detected during an evaluation of hydronephrosis identified prenatally or for sibling screening. Correlation was made with renal ultrasonography. We excluded infants with a history of urinary tract infection, evidence of ureteropelvic junction or bladder outlet obstruction as documented on intravenous pyelogram or voiding cystouretrogram (VCUG). All renal nuclear scans were reviewed by one radiologist (LC) while the corresponding sonograms were reviewed independently by another (CB). Of the 54 infants (28 boys and 6 girls) who met the criteria, VUR was bilateral in 25 and unilateral in 9. Thirty-eight of the 59 refluxing renal units had grade IV or V, 18 grade II or III and 3 grade I reflux. Median age at time of the DMSA renal scan was 2.2 months (range 0.5–5.8).

Results: DMSA renal scan identified parenchymal abnormalities in 65% (22) of the patients and 39% (23) of the refluxing renal units. The majority of these patients were male (19 compared to 3 female) and had bilateral VUR (15 compared to 7 unilateral cases). Differential uptake < 40% and cortical defects were seen in 10 refluxing units, differential uptake < 40% without cortical defects in 7 and cortical defects alone in 6. Of the 23 refluxing renal units with DMSA abnormalities, 20 were associated with Grade IV or V and 3 with Grade II or III. Interestingly, only 42% of the patients with an abnormal DMSA scan had sonographic evidence of a parenchymal abnormality.

Conclusions: We observed that of those children with high grade reflux in whom we had obtained DMSA renal scans, the majority had decreased differential function, cortical defects or both. Furthermore, not all those with renal parenchymal defects were identified by renal ultrasonography. These findings suggest that many infants with high grade VUR may have evidence of renal injury in the absence of bacteriuria and that DMSA renal scans, rather than renal sonograms alone, are useful in the follow-up care of these patients in assessing the detrimental effects of VUR on the kidneys.
NEONATAL VESICoureTERAL REFUX: NATURAL HISTORY

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Purpose: The use of obstetric ultrasonography (US) has identified a group of asymptomatic neonates who subsequently will be diagnosed with vesicoureteral reflux. Controversies still exist on both natural history and indications for intervention for this entity. In an attempt to further evaluate the natural history of neonatal vesicoureteral reflux, retrospective analysis of patients with antenatal history of hydronephrosis and documented reflux in the first 30 days of life was done.

Materials and Methods: Between 1993 and 1998, all patients who had a cystogram in their first 30 days of life associated with antenatal hydronephrosis in a children's hospital (n=260), patients with VUR secondary to infravesical obstruction and duplex systems were excluded. There were 31 (12%) patients with unilateral or bilateral refluxing renal units evaluated (54 renal units). The grade of ureteral reflux was correlated with ultrasonographic findings, spontaneous resolution of high grade reflux using the Kaplan-Meier survival curves, urinary tract infections, differential renal function of less than 35% on DMSA renal scan.

Results: The total number of patients was 31 (males 77%), the total number of refluxing units was 54 (males 80%). The distribution of the grades was as follows: Grade I: 5% (males 33%), Grade II: 15% (males 62%), Grade III: 32% (males 71%), Grade IV: 18% (males 90%), and Grade V: 30% (males 100%). Postnatal ultrasound findings correlated poorly with the presence and degree of VUR. Improvement was defined as a decrease in the grade of reflux of at least two grades on one side. Eleven patients (36%) did improve during a mean follow up period of 21 months. Six patients did not improve at a mean follow up of 14 months. Nine patients have not come for follow up. The duration of persistence of reflux for grades III, IV, and V was analyzed using the Kaplan-Meier estimate. The estimated duration for improvement of reflux grade III, and IV was 29 months and for grade V was 32 months. Two male patients had ureteral reimplantation for Grade IV unilateral reflux in one and bilateral grade IV in the other (follow up 19 months). The indications were query refluxing obstructing megalureter in the former, and failure of reflux to resolve in the later. Two female patients had a unilateral nephrectomy because of nonfunctioning renal units, one had a reflux grade I on the side of a dysplastic kidney and the other had a contralateral grade II reflux. Three male patients (10%) with bilateral grade V (6 renal units) reflux underwent vesicostomy at birth. On follow up (mean 22 months), two patients had ureteral reimplantation (3 renal units grade IV reflux). Eight patients (26%) had urinary tract infections while on antibiotics, 5 with bilateral grade V, 2 with at least unilateral grade V on one side, and 1 with grade I reflux into a nonfunctioning kidney. Twenty-three patients were evaluated, 12 renal units had less than 35% function on DMSA, the corresponding grade of reflux to that unit was: grade I: 8%, grade II: none, grade III: 26%, grade IV: 33%, and grade V: 33%.

Conclusion: Neonatal vesicoureteral reflux is characterized by a male preponderance and usually associated with a higher grade. A normal postnatal ultrasound should not be a basis for excluding the use of cystography. Our Kaplan-Meier estimate shows that high grade reflux may resolve spontaneously. The role of surgery (vesicostomy or reimplantation) in infants with antenatal hydronephrosis and reflux remains uncertain. Reflux nephropathy may be seen with both high grade and low grade reflux, high grade reflux is associated with a higher incidence of infection.

TREATMENT OF BLADDER DYSFUNCTION IN INFANTS WITH DILATING VESICoureTERAL REFUX

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There are several reports suggesting that dilating infant vesicoureteral reflux and bladder dysfunction are an entity, but still without proof for a causal connection. In older children the connection between bladder dysfunction and reflux is well known and treatment of the bladder is also accepted as beneficial for spontaneous resolution of the reflux. There are no reports about treatment of bladder dysfunction in infants with dilating VUR. This study preliminary presents treatment of bladder dysfunction in infants with dilating reflux.

Material: 17 infants (13 males and 4 females) of 103 infants (67 males and 23 females) with dilating VUR have been treated because of bladder dysfunction since 1992. The follow-up period was mean 2.7 years from start of treatment. All children were investigated both at presentation and follow-up with videocystometry and the 4-hour voiding observation. The treatment strategy included CIC (also had to be performed at hight if the morning volumes were high) and also early toilet-training since the emptying ability spontaneously increase when the child control his voiding habits. The indication for treatment was high bladder capacity and high volumes of residual urine in the free voiding studies (> 1/3 of bladder capacity), but only when seen together with recurrent UTI. The 13 male infants all had grade 5 reflux, bilateral in 90% (bilat grade 5 was seen in 45% in the non-CIC males). The 4 females had bilat grade 4. In those where the reflux had not downgraded significantly, surgical treatment was performed when the bladder function was under control but still on CIC treatment (between 2.5 and 4 years of age).

Results: In the CIC group bladder capacity at first investigation was mean 150% of normal in both males and females (non-CIC males 85% and females 117%). The voiding detrusor pressure was also higher in the CIC group (males 138 cm H2O, females 85 cm H2O) compared to those not on CIC (males 117 cm H2O, females 76 cm H2O). Residual urine in the CIC group was mean 40 and 37 ml in males and females, respectively. The corresponding volumes in those not on CIC was 10 and 15 ml. During the follow-up time the bladder capacity increased during the first year (260% of expected capacity) and residual urine in free voiding studies was unchanged. After toilet training residual urine decreased in 8 (7 males, 1 female). CIC was prematurely ended in one girl at the age of 1.5 years due to non-compliance. Six of the children were dry during nights from age one year. In those CIC also was performed once during night-time. Reflux resolved spontaneously only in one of the females (CIC ended), whereas in the remaining children no signs of spontaneous resolution was noted (non-CIC overall 38%). In 12 (10 males, 2 females) of the 17 children bilateral
neoureteral implantation was performed (at age 2.9 years) and CIC have been possible to end in 8 after surgery (7 males, 1 female). UTI recurrences were not seen after introduction of the treatment, except in one male infant.

**Conclusion:** Treatment of the incomplete emptying ability with CIC and after toilet training with addition of voiding regimen, do not seem to influence the rate of spontaneous resolution of severe reflux in infancy, but prevent problems with recurrent urinary tract infections. We suggest severe bladder dysfunction as a negative prognostic factor for reflux resolution, which have also been suggested by Young. The treatment must be look upon as an investment for a normalized bladder function, which may prevent those with the extremely high capacity bladders to have the lazy bladder problem in the future.

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**IS THERE RISK OF CONTRALATERAL REFUX AFTER PRIMARY OBSTRUCTIVE MEGAURETER REPAIR?**

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**Background:** It has been previously reported the disappointing onset of contralateral vesico-ureteric reflux (VUR) after unilateral successful repair of primary VUR. Different pathogenetic hypotheses and different surgical strategies have been proposed for this phenomenon which occurs in 10% to 27% of unilateral VUR repairs. Little attention has been spent to the behaviour of congenital obstructive megaureter (COM) in relationship with the onset of contralateral reflux after unilateral reimplantation with or without tapering.

**Methods:** Fifty-eight patients, aged from 2 to 10 years (mean: 3.2 years) underwent ureteral tapering and reimplantation for unilateral COM (42 left and 16 right side). Reimplantations were performed cross-trigonal in 57 cases and longitudinal according to Politano-Leadbetter in 1 case; 47 ureteral tapering were performed according to combined Hendren and Starr techniques and 11 were Kalicinski repairs. All patients underwent preoperative renal ultrasound (US), DTPA nuclear scan, pyelogram (IVP) and voiding cysto-urethrogram (VCUG) to rule out the presence of VUR. The control group is composed of 98 age-matched children with unilateral VUR who underwent unilateral reimplant with or without ureteral tapering. $\chi^2$ was used for statistical analysis.

**Results:** Follow-up ranges from 6 months to 4 1/2 years. All children of both groups underwent a VCUG 6 months postoperatively and US at 3-6-12 months follow-up. In the study group a newly developed contralateral reflux was detected in 1 child with COM who underwent a Kalicinski ureteral tapering and cross-trigonal reimplantation (1.7%). In the control group we had 11 cases of newly developed contralateral reflux (11.2%). The difference was statistically significant (p<0.005).

**Conclusion:** These results indicate that vesico-ureteral reimplantation for unilateral COM repair is not responsible of the onset of newly diagnosed contralateral reflux. The single case observed remains unexplained. In this regard COM behaves differently from primary VUR. The occurrence of contralateral reflux after successful unilateral VUR repair is significantly high (11.2%) and it is independent from age, sex and technique of reimplantation and/or ureteral tapering / plication. The difference between the study group (unilateral COM) and the control group (unilateral VUR) regarding the postoperative contralateral reflux onset is highly significant (p<0.005). Our results confirm the hypotheses that the functional anatomy of the trigone is preserved in primary megaureter, whereas the uretero-vesical junctions appear bilaterally impaired in VUR. Thus, the onset of contralateral VUR is not significant in COM repairs and seems a consequence of the primitive trigonal impairment in primary VUR, rather than the effect of the bladder fibers distortion during the ureteral reimplantation.

These results should differentiate the surgical strategy of primary VUR from COM.

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**BILATERAL EXTRAVESICAL URETERONEOCYSTOSTOMY (DETRUSORRHAPHY) IN CHILDREN: LIMITED RISK FOR POSTOPERATIVE URINARY RETENTION**

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**Background:** Although detrusorrhaphy is a popular surgical technique for correction of vesicoureteral reflux (VUR), concern over postoperative urinary retention often limits its utilization in cases of bilateral VUR. A series of consecutive detrusorrhaphy procedures is reviewed to better define the risk factors associated with this complication.

**Methods:** Clinical record of all children undergoing ureteroneocystostomy by a single surgeon over a ten year period beginning in January, 1989 were reviewed. Cases were stratified according to the technique used: either detrusorrhaphy or a transvesical procedure. Cases were further classified according to the age at surgery, and the grade of preoperative and postoperative VUR present, as well as for postoperative urinary obstruction or retention.

**Results:** Over the study interval, 101 detrusorrhaphy procedures (73 bilateral, 28 unilateral) were performed in 68 children, ranging in age from 7 months to 17 years old (mean age 6.0 years). These detrusorrhaphy procedures represented 32% of all ureteroneocystostomies performed (316), and accounted for 31% of bilateral cases (237), and 35% of unilateral cases (79). Ureteral duplication, neuropathic bladder dysfunction and megaureter accounted for only 6 patients undergoing detrusorrhaphy. Mean age at operation was similar for the bilateral (5.0 years) and the unilateral (6.4 years) detrusorrhaphy groups. All patients undergoing detrusorrhaphy had VUR to the renal pelvis documented on either a contrast or nuclear voiding cystourethrogram performed within 6 months prior to surgery. Neither ipsilateral nor contralateral VUR was detected on postoperative cystography for children undergoing detrusorrhaphy. Similarly, no postoperative obstruction or new significant hydronephrosis was discovered in this group. Minimal residual urine volumes were detected on postoperative cystography performed within 2 months of detrusorrhaphy.

Following detrusorrhaphy, a urethral catheter was maintained postoperatively for 2 days in 25 children (14 bilateral cases) during the first 5 years of this series, and only overnight in 43 children during the latter half (26 bilateral cases). Children were discharge from the hospital on the day that their urethral catheter was initially removed. Postoperative urinary retention requiring replacement of a urethral catheter was limited to only 3 children, all under going bilateral detrusorrhaphy (4% of bilateral cases). The mean age for these children was 11 months, and all 3 had bilateral high-grade VUR present preoperatively. All regained spontaneous efficient voiding after catheter drainage for 2 to 3 days. Two of these had their initial urinary catheter removed the day after surgery.

**Conclusions:** Detrusorrhaphy is a reliable technique for correcting either unilateral or bilateral VUR in children, which allows discharge to home predictably on the day following surgery. Postoperative VUR or ureteral obstruction is uncommon. Postoperative urinary retention may occur in up to 5% of bilateral cases, but is easily managed by a short course of urethral catheterization. Infants with bilateral high-grade VUR may present a greater risk to develop this complication.
KETOROLAC SUPPRESSES POSTOPERATIVE BLADDER SPASMS AFTER INTRAVESSICAL URETERAL REIMPLANTATION


Introduction: The precise mechanism by which postoperative bladder spasm occurs is not known, but there is evidence that increased prostaglandin synthesis via cyclooxygenase (COX) pathways plays a critical role in the pathogenesis of bladder spasm by sensitizing capsaicin-sensitive C-fiber neural afferents. Ketorolac tromethamine is an injectable form of COX inhibitors that has been shown to be an effective analgesic agent in various postoperative settings. This study was performed to test the hypothesis that ketorolac suppresses postoperative bladder spasms.

Patients and Methods: We designed a prospective study in which patients undergoing intravesical ureteral reimplantation for vesicoureteral reflux were randomized in a double-blinded fashion to receive either ketorolac or placebo postoperatively. Twenty-four patients (22 girls, 2 boys) were enrolled into the study after obtaining an informed consent. Their ages at the time of operation ranged from 4 to 11.5 years (mean 5.9). Patients with a history of voiding dysfunction or constipation were excluded. Twelve patients were assigned to each group. The patients in both groups shared similar preoperative characteristics in terms of mean age (6.1 vs. 5.8 years), bilaterality of reflux (83% vs. 91%), and mean reflux grade (2.4 vs. 2.5). All patients were maintained on an epidural infusion of bupivacaine (0.1%) with fentanyl (2 mcg/cc) throughout the study. Patients were given either ketorolac (0.5 mg/kg/dose) or placebo (saline) intravenously at the conclusion of surgery and every 6 hours thereafter for 48 hours. Patients were instructed to record bladder spasm episodes prospectively on a standardized time-flow diary using the following scoring system for spasm severity: 1-mild, 2-moderate, and 3-severe. The percentage of patients experiencing bladder spasms was compared between two groups using Fischer’s exact test. The mean total number of bladder spasm episodes and the mean severity score were compared using Wilcoxon non-parametric test.

Results: Patients receiving ketorolac experienced significantly fewer bladder spasms compared to those receiving placebo. Three out of 12 patients (25%) in the ketorolac group experienced bladder spasms, compared to 10 out of 12 patients (83%) in the placebo group (two-sided p = 0.012). Patients in the ketorolac group experienced a mean of 1.9 episodes of bladder spasms, compared to those in the placebo group who experienced a mean of 5.9 episodes (p = 0.002). The mean severity score for the ketorolac group was 1.6 (maximum score 3.0), compared to 2.6 for the placebo group (p = 0.003). No patient developed adverse effects related to ketorolac use during the study.

Conclusions: The findings from this study clearly demonstrate that ketorolac reduces the frequency and severity of bladder spasms after intravesical ureteral reimplantation. Our findings also support the postulate that increased prostaglandin production via COX pathways is an important mechanism by which bladder spasm occurs.

ARE POST-OPERATIVE STUDIES JUSTIFIED AFTER EXTRAESVEICAL URETERAL REIMPLANTATION?

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Introduction: Primary vesicoureteral reflux (VUR) is common and most often resolves spontaneously. When indicated, surgical correction is highly effective. The extravesical reimplantation (modified Lich-Gregoir) with its low morbidity, has recently gained a wider acceptance. Post-operative evaluation routinely includes a voiding cystogram (VCUG) and an ultrasound (U/S) done at 6 weeks and 12 weeks respectively. We speculate that these studies could be avoided in a large subset of patients, thus reducing patient discomfort and adding significant socioeconomic benefits. Recent studies with intravesical approaches have explored that aspect without clearly identifying indications for post-operative evaluation.

Purpose: To evaluate the need for post-operative VCUG and U/S and identify subsets of patients in which these studies are necessary.

Methods: We reviewed records of 438 patients from 2 institutions treated for vesicoureteral reflux using an extravesical approach between 1991 and 1997. All were operated by specialty trained pediatric urologists. Inclusion criteria were patients with primary reflux not undergoing other concomitant surgery with at least 1 year of post-operative follow-up. Patients with pre-operative voiding dysfunction are included. The indication for surgical intervention was unresolved reflux (>4 years) in more than 70% of patients. Other indications include breakthrough urinary tract infections, progressive parenchymal scarring, non-compliance to medical treatment. Post-operative evaluation included a VCUG at 3 months and at 12 months if reflux was unresolved at 3 months. Also an U/S performed at 6 weeks or earlier if clinically indicated and at 12 months.

Results: 438 patients underwent extravesical ureteral reimplantations either unilaterally (n = 130) or bilaterally (n = 227) for a total of 723 ureteral units. The distribution of ureteral units reimplanted is 34 grade 1, 190 grade 2, 285 grade 3, 171 grade 4, 32 grade 5 reflux and 11 non-refluxing units. All non-refluxing ureters, all grade 1, and 91.1% of grade 2 reflux were reimplanted in bilateral procedure. Overall success rate at 3 months and 12 months were 93.2% and 96.8% respectively. There were 49 ureteral units refluxing at 3 months, of which 38 were ipsilateral and 11 contralateral. At 12 months 20/38 ipsilateral reflux and 8/11 contralateral reflux had resolved spontaneously. Of the 18 ipsilateral reflux remaining at 1 year, 12 were from ureters with pre-operative high grade reflux of which were ongoing high grade (4 & 5) post-operatively. There was a statistically significant difference in success rate at 1 year (p < 0.007) between high grade (94%) versus low grade (99%) pre-operative reflux. Univariate analysis looking at gender (male vs. female), age (2 vs >3) and pre-operative bladder function (dysfunctional voiding vs. normal bladder function) revealed no significant differences in success rates. Post-operative hydronephrosis (SFU grade 1, 2 or 1 increment in grade from pre-operative status) was observed in 7.2% of ureteral units at 6 weeks and in 0.005% at the 12 months follow-up visit. No cases of high grade hydronephrosis were observed. Five patients had clinical evolution in the early post-operative period requiring U/S evaluation of the kidneys (3 increased creatinine, 1 high blood pressure and 1 flank pain) and all had significant hydronephrosis that resolved without intervention in 4 (1 redo reimplant).

Conclusion: Extravesical reimplantation is highly effective in treating VUR. Post-operative VCUG can be safely avoided in low grade reflux and should be reserved for high grade reflux. U/S
should be done only if clinically indicated or for indications other than hydronephrosis. Limiting these studies would help reduce patient discomfort and also have substantial socioeconomic benefits.

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EXTRAPERITONEAL ENDOSCOPIC NEPHRECTOMY IN INFANTS AND CHILDREN

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Currently, endoscopic nephrectomy in children is performed either from anteriorly through a transperitoneal laparoscopic approach or from posteriorly through a retroperitoneoscopic approach. The former approach necessitates transgression of the peritoneal cavity and usually mobilization of the colon, while the posterior retro-peritoneoscopic approach suffers from lack of operative space and crowding of working instruments.

Objective: To evaluate the effectiveness of a lateral extraperitoneoscopic approach for nephrectomy in infants and children.

Patients and Methods: Twelve patients had extraperitoneal endoscopic nephroureterectomy or hemic- or nephroureterectomy (5 cystic dysplastic kidneys, 4 reflux nephropathy, 2 non-functioning, upper moieties of duplex kidneys, 1 non-functioning kidney due to pelviureteric junction obstruction) performed at a mean age of 3.8 years (range: 7 months-9.2 years). Through a 1 cm incision made midway between the anterior iliac spine and the 12th rib, the retroperitoneal space was entered and then enlarged with balloon dissection under endoscopic control through a 5 mm port. Two more 5 mm working ports, one anterior and the other posterior to the camera port, were inserted under endoscopic guidance. The kidney, enclosed by the Gerota's fascia, and its draining ureter, could be approached from anteriorly with ease. The renal vessels were usually coagulated and divided with bipolar forceps or ultrasonic scalpel without the use of clips.

Results: Extraperitoneoscopic nephrectomy or hemic-nephroureterectomy was successfully performed in all twelve patients. The mean operating time was 89 minutes (range 40-185 minutes). All patients recovered uneventfully and no procedure-related complication was encountered.

Conclusion: This lateral extraperitoneoscopic technique for nephrectomy and hemic-nephroureterectomy is simple, safe and effective in infants and children, and allows much more operating space and freedom of movement of instruments than the posterior retroperitoneoscopic technique. By staying out of the peritoneal cavity, the risk of injury to intraperitoneal organs is minimized.

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LAPAROSCOPIC RETROPERITONEAL NEPHRECTOMY IN HIGH RISK CHILDREN

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Background: Nephrectomy may be indicated in children with end stage renal disease to control hypertension or severe coagulopathy. We have studied the feasibility and the results of nephrectomy done by retroperitoneal laparoscopic approach in these high risk children.

Methods: We have performed 22 nephrectomies by retroperitoneal laparoscopy during 1997 and 1998. The last 12 cases had end stage renal disease and were under dialysis program. Our study includes this last group. Mean age was 7 years (7 months to 13 years). Nephrectomy was done through a retroperitoneal approach, lateral position, using a main port of 10 mm and 2 access-
sory ports of 5 mm. Renal artery and vein were ligated separately by endocorporal knots and clips. Kidney was retrieved through the main incision in all cases, in 2 cases a laparoscopic bag was used. The mean size of kidney was 8 cm (5 to 12 cm). Nephrectomy was bilateral in 2 cases (7 and 12 months). Drainage was left in the last 6 cases.

Results: The procedure was feasible in all cases without conversion. Mean operative time was 2 hours (1h20m to 3h10m). No intraoperative infection has occurred, pneumoperitoneum was produced in 3 cases without complications. One child had postoperative hemotoma which resolved spontaneously. Hemodialysis was started on the first postoperative day. Feeding was started on the second postoperative day. Analgesia was obtained by paracetamol and nalbuphine, morphine was necessary in 5 cases. Mean hospital stay was 2.2 days (3 to 7 days).

Conclusion: Retroperitoneal laparoscopic nephrectomy is safely feasible in high risk children. The relative long operative time is needed to obtain an optimal conditions to ligate safely the renal pedicle. The absence of major complications may be explained by the fact that the learning phase was done first on relatively easier nephrectomy, for obstructive uropathy, before proceeding in high risk children.

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IS RETROPERITONEAL RENAL BIOPSY ALTERNATIVE TO PERCUTANEOUS NEEDLE AND OPEN BIOPSIES?

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Background: Renal biopsy continues to be a pivotal tool in the clinical assessment of persistent microscopic hematuria, proteinuria, hypertension and other renal diseases. The percutaneous needle biopsy is the first choice procedure. Unfortunately, some clinical conditions, such as severe hypertension, bleeding disorders, anticoagulation medications, anatomical abnormality and very young age children reduce the use of the percutaneous approach in favor to the open surgery. We think that retroperitoneal laparoscopic biopsy is a suitable alternative.

Patients and Methods: From January 1998 to March 1999 we performed retroperitoneal laparoscopic biopsy in 22 patients, aged 2 to 22 years (mean age: 12 years). Preoperative indication to renal biopsy included 7 significant proteinuria, 4 persistent hematuria, 3 systemic hypertension, 6 renal failure and 2 Shoenlein-Henoch syndrome. The retroperitoneal approach is performed with the patient in lateral position. Two trocars are used: the first, a 10 mm trocar, is positioned under direct vision (Visiport®) along the posterior axillary line of lumber region and a 15 mmH2O pressure is set up. A blunt dissection of the retroperitoneal virtual space is carried out before positioning the second trocar (5 mm diameter), 3 to 5 centimeters medially to the first one. As the lower renal pole is freed from the fat tissue, biopsy forceps are used to grasp the parenchymal specimen. Bleeding control is ensured under direct vision, if necessary fulgurating the biopsy site with bipolar electrocoagulancy.

Results: Retroperitoneal laparoscopic biopsy was successfully performed in 21 patients. One 19 years old boy was converted in open surgery during the procedure for difficult endoscopic identification of the kidney (obesity). The mean operative time was 50 minutes (range from 30 mins to 110 mins). In all patients blood loss was minimal and the mean hospital stay was 1.3 days postoperatively. One minor intraoperative complication occurred in this series (a small peritoneal opening) without postoperative consequences. No pain medication was required after hospital discharge and the patients were back to their usual activity in 4 to 6 days.

Conclusion: The retroperitoneal laparoscopic biopsy is a simple and safe technique for renal biopsy in childhood. It is required a not extensive laparoscopic experience and provides a good paren-
chymal specimen. We believe that the retroperitoneal approach has less morbidity than open surgery and it is the first choice technique in pediatric patients when percutaneous needle biopsy is contraindicated or not suitable.

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LAPAROSCOPIC SURGERY IN CHILDREN WITH VENTRICULOEPITONEAL SHUNTS IS NOT ASSOCIATED WITH CONSEQUENCES OF INCREASED INTRACRANIAL PRESSURE

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Background: Based on shunt pressure measurements in two children during pneumoperitoneum, it has been suggested that patients with ventriculoperitoneal (VP) shunts are at risk for increased intracranial pressure and brain herniation. Based on this experience, pressure monitoring of the shunts and ventricular drainage to maintain a normal pressure has been recommended. A large series of patients with VP shunts undergoing laparoscopic surgery was studied for clinical indications of increased intracranial pressure.

Methods: The medical records of 18 patients with VP shunts undergoing 19 consecutive laparoscopic operations were reviewed for clinical evidence of increased intracranial pressure. Anesthesia records were reviewed for operative time, CO2 levels, pulse, blood pressure and any untoward anesthetic events. All data points were recorded in a computerized database, and analyzed for evidence of combined hypertension and bradycardia. Postoperative records were scanned for evidence of neurological changes, especially relating to midbrain function.

Results: There were 12 females and 6 males, with a mean age of 13.2 years. Procedures performed included laparoscopic VP shunt revision (1), two-stage laparoscopic orchidopexy (2), laparoscopic and laparoscopic-assisted reconstructive procedures (16). Mean operative time was 7 hours, 13 minutes, with an estimated mean laparoscopic time of 2 hours 52 minutes. There were no instances of significant bradycardia/hypertension (defined as systolic pressure, diastolic pressure, or pulse two standard deviations from the mean for age), no evidence of a trend to combined bradycardia and hypertension during pneumoperitoneum, and no untoward anesthetic events. The complete anesthesia record was not available in two of the 19 procedures. All were examined on at least one occasion postoperatively by a pediatric neurologist and/or neurosurgeon, and there was no evidence of neurological deterioration in any patient with the exception of one girl with a cervical syrinx, which progressed over the two years after surgery. Three patients have subsequently undergone VP shunt revision, with no apparent relationship to the laparoscopic approach. Mean follow up for the group is 15.3 months, ranging from 1 to 58 months.

Conclusion: There is no evidence of clinically significant increased intracranial pressure in this substantial series of patients with VP shunts undergoing laparoscopy. Unless further clinical information should suggest otherwise, monitoring of intracranial pressure is not necessary during laparoscopic procedures in the patient with a VP shunt.

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VARIABILITY OF SIGNIFICANCE OF NUCLEAR MEDICINE CYSTOGRAM


Introduction: Radionuclide cystography (RNC) is a widely used test in the diagnosis or as an indication of resolution, of vesicoureteric reflux (VUR). The recurrence (persistance) of reflux after one negative RNC has been previously reported. This prospective study further elaborates on this phenomenon.

Materials and Methods: 85 patients with primary VUR, treated conservatively, between 1991 and 1996 having one negative RNC, were included in this study. 12 to 18 months after the negative study a repeat RNC was done. Two groups, those with and those without recurrence of reflux were identified and compared as to sex distribution, age of presentation, age of resolution, time between presentation and first negative RNC, change in grade be-
between presentation and just before resolution, side of reflux at presentation and grade before resolution. The differences between both groups were statistically analyzed.

Results: Of the 85 patients, 25 (29%) had recurrence of reflux. Of these, 18 (72%) patients had recurrence with grade two or greater, and 15 (60%) of the 25 patients are still refluxing 12 months after the second positive RNC. There was no observed association between the two groups in any of the variables (p-values were greater than 0.05).

Discussion: This study emphasizes the importance of a second negative RNC to indicate absence/resolution of reflux, as one negative RNC alone would have missed persistent reflux in 25 of 85 patients at one year and 15 of 85 patients at two years. Whether this is variability in the disease process or an unknown factor inherent in the test is unknown, in that there is no statistical difference in the parameters studied between the two groups.

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SHOULD THE PERFORMANCE OF THE VCUG BE BASED ON RACE IN THE EVALUATION OF PRENATAL HYDRONEPHROSIS?

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Introduction: The prenatal detection of hydronephrosis is now a common occurrence due to the routine performance of obstetrical ultrasound screening. Generally, postnatal evaluation has included a postnatal renal/bladder ultrasound and voiding cystourethrogram. Due to the high incidence of vesicoureteral reflux in the Caucasian population and low incidence in the African-American population, some have advocated that the VCUG be omitted in the postnatal evaluation of the African-American patient with prenatal hydronephrosis. We reviewed our experience in 1019 patients.

Methods: We reviewed our database which consisted of 1019 patients with prenatal hydronephrosis. We collated the data with regards to postnatal testing and ethnicity.

Results: There were 1019 patients enrolled in our prenatal hydronephrosis database. 81% of patients (830/1019) underwent VCUG testing. Ethnicity data on the entrance prenatal hydronephrosis form was optional. We have ethnicity data on 311 of the 830 patients tested. African-Americans make up 27/311 (8%) of this group, Hispanics 9%, Asians 3%, and Caucasians 83%. Of the 830 tested, 339 had a positive cystogram and ethnicity data was available on 100 (136 declined to answer, unknown in 3). We found the following:

<table>
<thead>
<tr>
<th>Positive Cystogram Group (N = 100)</th>
<th>Within Ethnic Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>African-Americans</td>
<td>4%</td>
</tr>
<tr>
<td>Hispanics</td>
<td>4/27 (15%)</td>
</tr>
<tr>
<td>Asians</td>
<td>6%</td>
</tr>
<tr>
<td>1/10 (1%)</td>
<td></td>
</tr>
<tr>
<td>Caucasians</td>
<td>89%</td>
</tr>
<tr>
<td>89/227 (35%)</td>
<td></td>
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</tbody>
</table>

In the 4 African-American patients with reflux, the grade ranged from 2 to 4 while the degree of hydronephrosis ranged from 0–3. The ultrasound grading was none (0), mild (1), mild-mod. (2), mod. (3), mod.-sever (4), and severe (5).

Conclusions: The incidence of vesicoureteral reflux in African-Americans with a history of prenatal hydronephrosis is sufficient to continue recommending the performance of postnatal voiding cystourethrogram. Due to the small sample size of the Asian population, no conclusions can be drawn in regards to this population. Therefore we recommend continued VCUG evaluation in all patients with prenatal hydronephrosis.

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PREDICTION OF OUTCOME IN THE MANAGEMENT OF VESICOURETERAL REFUX: ROLE OF NEURAL NETWORKS

Satbir Singh MD, Umesh Patil MD FAAP, Steven Docimo MD FAAP, Ranjiv Mathews MD FAAP. Syracuse, N.Y. & Baltimore, MD. (Presented by Dr. Singh)

Background: The current initial management of vesicoureteral reflux (VUR) consists of antibiotic prophylaxis and radiographic follow-up. Surgical correction is reserved for children 1) who develop recurrent urinary tract infections (UTI) despite adequate antibiotic prophylaxis; 2) those unable to tolerate antimicrobial prophylaxis, or 3) do not resolve despite protracted follow-up. Prior studies have demonstrated that better prediction of resolution would enhance patient management and reduce costs. Artificial neural networks (ANN) have been used successfully for the prediction of outcomes in many medical applications. An artificial neural network was designed to assist with outcome prediction in children with vesicoureteral reflux.

Methods: Charts of 163 patients with VUR were reviewed. Data collected included laterality, grade of reflux at diagnosis, patient sex and outcomes—surgery or resolution. A commercially available neural network (Backpack™, Z Solutions, Atlanta) was modified for this application. The patient population was divided into a training set (98 patients) and a test set (65 patients). The ANN was trained using the training set and then used to predict outcomes of the test set.

Results: Once appropriately trained the ANN was able to achieve an overall predictive accuracy of 85%. This reflected a 92% accuracy in predicting patients that had resolution of reflux and 80% in predicting patients that went on to surgical correction. When reflux grade was considered, the ANN was able to predict outcomes in 100% of grades I, IV and V. Accuracy in predicting outcomes in grades II and III was 80%.

Conclusions: Improved prediction of outcomes (resolution or persistence) in children with reflux will allow better management and decrease costs. This is particularly important in the intermediate grades of reflux (II and III). The ANN was able to reliably predict outcome in 80% of children with intermediate grade reflux and may be a valuable tool in tailoring management.

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VESICOURETERAL REFUX DYSREGULATES THE RENIN-ANGIOTENSIN SYSTEM IN THE FETAL SHEEP KIDNEY

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Introduction: Previous studies have indicated that the renal renin-angiotensin system (RAS) is upregulated in response to obstruction. Specifically, renin and angiotensin II gene expression is increased in the obstructed renal cortex. It has been suggested that the activation of RAS results in the increased expression of TGF-β, a potent fibrogenic factor. TGF-β in turn, can induce the activation of tissue-inhibitor metalloproteinases (TIMPs) expression. Consequently, alteration in RAS may lead to changes in extracellular matrix composition (ECM), as seen in interstitial fibrosis. While alterations in the RAS have been characterized in the obstructed kidney, little is known regarding its role in reflux nephropathy. In this study, we investigated whether sterile reflux induces specific alterations in the RAS expression pattern.

Methods: Prenatal vesicoureteral reflux was surgically created in fetal sheep at 95 day of gestation. At birth, the animals were immediately placed on antibiotic prophylaxis. At time of
sacrifice (5.5 to 10 months of age), the animals were assessed for infection (urine cultures), renal scarring (DMSA scan) and the presence of VUR (VCUG). Samples were obtained from the renal cortex of animals with continued VUR \( (n=2) \), those in which reflux had spontaneously resolved \( (n=2) \) and those that underwent sham operations \( (n=2) \). Histochemical analysis was performed to assess for the presence of interstitial fibrosis. Semi-quantitative RT-PCR was used to quantify the levels of renin, angiotensinogen, TGF-\( \beta \), and TIMP-I mRNA (normalized to GAPDH mRNA levels).

**Results:** In kidneys in which reflux was created prenatally, three out of four had renal scarring. All of these had histologic evidence of interstitial fibrosis and a coordinate increase in the levels of renin, angiotensinogen, TGF-\( \beta \) and TIMP-I mRNA. The observed increased expression of these genes occurred not only in kidneys that had persistent reflux but even more so in those in which reflux had spontaneously resolved.

**Conclusion:** Kidneys that manifested a high degree of scarring showed marked increase in renin, angiotensinogen, TGF-\( \beta \) and TIMP-I mRNA expression. Our findings suggest that sterile reflux can cause an upregulation of the RAS which in turn, may lead to the expression of other genes such as TGF-\( \beta \) and TIMP-I; these genes can markedly alter the composition of the ECM, resulting in interstitial fibrosis. Pharmacologic blockage of the RAS may be helpful in preventing fibrosis associated with reflux nephropathy.

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**CONGENITAL VESICOUETERAL REFUX IN SHEEP IS ASSOCIATED WITH REDUCED EXPRESSION LEVELS OF AQUAPORIN-1 AND AQUAPORIN-2 IN KIDNEY INNER MEDULLA**

**Background:** Impaired concentrating capacity has been demonstrated in human refluxing kidneys and in growing animals with experimental congenital reflux (VUR). Aquaporin waterchannel proteins are the principle mediators of water homeostasis in the kidney. This study assesses the impact of VUR on renal aquaporin protein levels.

**Methods:** Fetal VUR was surgically induced in 6 male, fetal sheep at 95 days gestation (term 140 days). After birth, animals received antibiotic prophylaxis and reflux grades were assessed by fluoroscopic voiding cystogram. Concentrating capacity was assessed by dDAVP test at 1 month and 6 months. 3 normal age and sex matched controls were studied at each timepoint. After sacrifice at 6 months \( (n=5) \) refluxing and \( n=3 \) normal kidneys were retrieved and frozen in liquid nitrogen. The midportion of the kidneys was divided into inner medulla, outer medulla and cortex. The inner medulla was assessed for AQP-1 and AQP-2 expression levels by quantitative immunoblotting using polyclonal rabbit antibodies.

**Results:** Mean maximal increase in urine osmolality after dDAVP stimulation was significantly lower at the age of 1 month in refluxing kidneys than normals and worsened by 6 months to 53 mosm/L (4-201) vs 628 mosm/L (151-1174) \( \text{In normal animals} \ (p=0.038). \) AQP1 expression level measured by densitometry was decreased in 4 out of 5 refluxing kidneys to a mean 0.27 (SD 0.23) vs 1.0 (SD 0.13) \( (p=0.006). \) Mean AQP2 expression in 4 out of 5 refluxing kidneys was 0.21 (SE 0.20) vs 1 (SE 0.17) in normal kidneys \( (p=0.0053). \) The kidney of one animal showed normal AQP1 and AQP2 expression levels.

**Conclusion:** Experimental fetal reflux progressively impairs renal concentrating capacity over 6 months of follow-up. Decreased levels of AQP1 and AQP2 appear to be critical determinants of this renal functional defect induced by sterile reflux.

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**EXPRESSION ARRAY "GENE CHIP" ANALYSIS OF IN VITRO UROTHELIUM EXPOSED TO UROPATHOGENIC ESCHERICHIA COLI PD1**

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**Background:** The urothelial response to infection has not been well studied at a molecular level. Urothelium is known to produce interleukins 6 and 8 in response to infection. However, other mucosal surfaces (i.e. pulmonary and intestinal epithelium) have been shown to have a highly specialized immune system. We conducted the following experiments to explore the hypothesis that the urothelium is also involved in a specialized mucosal immune system.

**Methods:** We exposed transformed (T24) and primary human urothelium to a chloramphenicol resistant clonal strain of *Eschericha coli* (PDC1) which is a known uropathogen. We isolated RNA and purified mRNA from the urothelium after 0 and 4 hours of exposure to PDC1. We then performed reverse transcription polymerase chain reaction (RT-PCR) and hybridized the products to a cDNA human expression array with 688 known expressed tag sequences.

**Results:** Exposure to E. coli (PDC1) produces a vigorous urothelial cytokine response in both primary and transformed urothelium. We found upregulation of chemokines that function to attract macrophages and polymorphonuclear cells (i.e. IL-6, neutrophil activating protein). mRNA for apoptosis-associated proteins (i.e. CD-27, NIP-3, apopain), DNA synthesis and repair proteins (i.e. replication factor C, DNA topoisomerase II), and stress response proteins (i.e. MAPK6, SAPK, heat shock proteins) are also upregulated along with extracellular signaling and communication factors. Transformed and primary urothelium generated quantitatively different responses to E. coli exposure.

**Conclusions:** Urothelium does not act only as a passive barrier to bacterial pathogens but appears to initiate and play an active role in response to infection involving chemotaxis, cell signal transduction, and programmed cell death. These findings suggest that the urinary tract possess an innate complex mucosal immune defense mechanism like other mucosal surfaces.

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**THE INDUCTION OF NITRIC OXIDE SYNTHASE IN HUMAN BLADDER SMOOTH MUSCLE CELLS BY INFLAMMATION: A POTENTIAL MECHANISM FOR FIBROSIS**

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**Background:** Nitric oxide (NO) is generated by nitric oxide synthase (NOS) and has been shown to be a multifunctional molecule in a variety of tissues. One of the isoforms, termed the inducible NOS (iNOS) is not typically expressed in normal tissues but has been demonstrated in various organ systems to be upregulated under inflammatory conditions leading to the release of large amounts of NO and formation of cytodestructive free radicals (peroxynitrite). The purpose of our study is to biochemically and molecularly characterize iNOS and its physiological effects during inflammation in cultured human bladder smooth muscle cells (SMC).

**Methods:** Primary human bladder SMC were cultured in Clonetics smooth muscle growth medium-2. Inflammatory conditions were simulated by adding a cytokine mixture (CM) containing lipopolysaccharide (E. coli), interleukin 1B, γ-interferon, and...
and tumor necrosis factor-α, iNOS expression was examined by RT-PCR. Northern and Western blot analyses and nitrite and nitrate levels were measured by the Griess reaction. Expression of extracellular matrix (ECM) proteins was examined by Western blotting.

Results: RT-PCR and Northern blot analysis demonstrated a significant increase in iNOS mRNA after cultured human bladder SMC were treated with CM, whereas untreated SMC remained negative for iNOS expression. Similar results were observed when iNOS protein expression was assessed by Western blot analysis. Measurement of nitrite + nitrate production, an end-point marker of functional iNOS activity, also revealed a significant time dependent increase in nitrite + nitrate levels in the CM treated bladder SMC when compared to the controls (29.87 μM vs. 14.35 μM @ 12 hrs, p ≤ 0.01). Nitrite + nitrate production in the CM treated group was noted to be inhibited by the selective iNOS antagonist aminoguanidine. In order to further explore the role of inflammatory stimuli and iNOS in the bladder, we assessed the temporal expression of ECM proteins in CM treated and untreated SMC. Western blot analysis revealed that CM stimulated type III collagen expression, a characteristic marker of fibrosis, in human bladder SMC. Furthermore, inflammatory stimuli of these bladder SMC resulted in the downregulation of protein expression for matrix metalloproteinase (MMP-1) and tissue inhibitors of metalloproteinase (TIMP-1), a scenario compatible with inhibition of remodeling and repair. Meanwhile the group control demonstrated a time-dependent increase in the expression of these remodeling proteins (MMP-1 and TIMP-1).

Conclusions: Primary human bladder SMC can be induced to express iNOS under inflammatory conditions in an in-vitro system. This induction of iNOS is also accompanied by the expression of type III collagen which is a characteristic marker for fibrosis. In addition, there appears to be a lack of ECM remodeling further contributing towards bladder fibrosis. Because of the cytotoxic nature of NO liberated by iNOS and the associative changes of fibrosis demonstrated in our study, we believe that this induction of iNOS may be a responsible mechanism for developing bladder wall fibrosis in the setting of chronic urinary tract infection.

Source of Funding: Eli Lilly Research Laboratories

GROWTH INHIBITION OF E. COLI BY THE URINE OF CHILDREN WITH URINARY TRACT ANOMALIES UNDER PROPHYLACTIC ANTIBIOTICS

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Background: Prophylactic antibiotics (PA) are accepted therapy for recurrent urinary tract infection in children with underlying urinary tract anomalies (UTA). They are usually administered once daily (in evening hours) over a prolong time period. Various agents have been used differing in their absorption, volume of distribution and half life.

Methods: This study examines the growth inhibition (GI) of E. Coli in the urine of 53 children with UTA given PA at a fixed evening hour. The children were divided into 4 group according to the type of antibiotic used:

<table>
<thead>
<tr>
<th>Treatment</th>
<th># of Patients</th>
<th>Stone Size in mm. Mean (Range)</th>
<th>Age (Mean Years)</th>
<th>Success Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ureteral Stent</td>
<td>2</td>
<td>2 (1–2)</td>
<td>13</td>
<td>100% (2/2)</td>
</tr>
<tr>
<td>Ureteroscopic</td>
<td>12</td>
<td>4 (1–10)</td>
<td>12</td>
<td>83% (10/12)</td>
</tr>
<tr>
<td>Lithotripsy</td>
<td>Shock Wave</td>
<td>Lithotripsy</td>
<td>2</td>
<td>7 (4–10)</td>
</tr>
</tbody>
</table>

On the following day, urine samples were collected in the morning, afternoon and evening. Samples were frozen at -70°C until tested. In order to quantitate GI, 50–250μl aliquots were inoculated onto wells created on an agar plate coated with E.Coli ATCC 35/218 (0.5 McFarland). The inhibition (in %) was compared to that obtained by the standard antibiotic disc (diffusion agar disc method). The urine volume which showed the same degree of inhibition as that obtained by the disc was taken as representing an equal antibiotic concentration to that of the disc. This urine volume (specific to each antibiotic) was then used to assess GI. Specific gravity (SG) and GI were determined on each urine sample.

Results: In children aged ~24 mths, urine concentration (UC) was found to be higher in the morning (SG 1.021± 0.006 am vs 1.008±0.004 pm, p<0.05). In contrast, in children aged >4y, UC was higher in the afternoon and evening hours (SG 1.019±0.003 pm vs 1.007± 0.003 am, p<0.005). Percentage urine samples demonstrating GI among groups was 20, 12, 75 and 82% for NA, CPT, CTM and CFX, respectively (p<0.001 for CTM/CFX vs NA/CPL).

Conclusion: UC during the day is dependent on the child’s age. The greater the degree of UC, the better GI. Duration of GI is dependent on the T1/2 of the antibiotic used. Both CPT and CFX afford adequate coverage for ~75% of a 24 hour day. A direct correlation was found between UC and GI (R=0.68, p<0.01).

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MANAGEMENT OF DISTAL URETERAL STONES IN CHILDREN—SIMILARITIES TO AUA GUIDELINES IN ADULTS

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Background: The AUA (American Urological Association) has published clinical guidelines for the management of ureteral calculi in adults (J. Urol. 1997, 158:1915–21). They found that up to 98% of stones less than 5 mm. in diameter will pass spontaneously. Ureteroscopy and shock wave lithotripsy were acceptable treatment choices for stones less than 10 mm in diameter in the distal ureter. We reviewed our management of distal ureteral stones in children to see if the AUA guidelines for adults apply.

Methods: Twelve males and 16 females (mean age 12 years, range 4 to 17 years) presented in the last 6 years with renal colic and distal ureteral obstruction. Intravenous urography was performed in 27 cases, and the mean stone size was 3 mm. (range 1 to 10 mm.). Most patients were treated with a 6.9 Fr. semi-rigid ureteroscope, however, more recent cases were done with a 4.5 Fr. needle ureteroscope.

Results: Twelve patients (42%) with a mean age of 11 years and a mean stone size of 2 mm. (range 1 to 3 mm.) passed stones spontaneously with intravenous hydration and narcotics. The mean follow-up in this series was 2 years.
Eighty seven percent (14/16) patients were successfully treated and all of them were stone free at the end of the procedure. The inability to pass a ureteroscope and a ureteral perforation account for the 2 attempts at ureteroscopic lithotripsy which were not successful. (*Of whom presented with urosepsis and underwent emergent percutaneous nephrostomy tube drainage.*) The stone composition in this group was predominately calcium oxalate.

Conclusions: Similar to the AUA guidelines in adults most stones less than 3 mm. in diameter in the distal ureter in children will pass spontaneously. Ureteroscopy and ESWL have a high success rate for stones between 4 and 10 mm. in the distal ureter. Needle ureteroscopes have allowed more stones to be treated safely and effectively in smaller children.

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THE URETEROSCOPIC TREATMENT OF PROXIMAL URETERAL AND INTRARENAL COLLECTING SYSTEM CALCULI IN THE PEDIATRIC POPULATION

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Introduction: The treatment of urinary calculi has evolved due to the development of miniature endoscopes and laser lithotripsy. Shock wave lithotripsy (SWL) is considered the first line treatment for most upper collecting system calculi. Ureteroscopy has been shown to be safe and effective in adults but large scale data regarding its use in children is yet to be accumulated. Presented here is our initial data regarding the endoscopic treatment of proximal ureteral and intrarenal calculi in children.

Methods: Patients who have undergone ureteroscopy for treatment of proximal calculi are presented. Indications for intervention include acute obstruction, nonspontaneous passage, persistent gross hematuria, and significant stone burden. When necessary, holmium laser lithotripsy was utilized. Postoperatively all patients were evaluated by either intravenous pyelogram, ultrasound, or abdominal x-ray to assess for changes associated with their treatment. All procedures were performed with either a 6.9 Fr minirigid or 7.4 Fr flexible ureteroscope.

Results: Twelve patients (8 male, 4 female) underwent 18 procedures (10 ureteral, 8 renal) from 7/97 to 12/98. Mean age was 9.0 years (13 mos.-17yrs); 9 were prepubertal and 3 postpubertal. One patient has primary hyperoxaluria and one primary hyperparathyroidism requiring multiple procedures until metabolically controlled. One patient has a history of a prior bilateral Cohen ureteral reimplantation. All patients were done on either an outpatient (14) or overnight (4) basis. 5/18 required dilatation prior to placement of the flexible ureteroscope (3 graduated dilator, 2 balloon). Ten/10 ureteral calculi were successfully removed with one treatment. Six/8 (75%) renal calculi were successfully treated with ureteroscopy. One failed due to mechanical trouble (breakdown of laser and failure of electrohydraulic lithotripsy) and required auxiliary SWL; one radiolucent lower pole calculus could not be engaged for endoscopic lithotripsy or removal. Five/6 renal stones were cleared at the initial setting. All patients had stents postoperatively, 15/18 with a dangler string to facilitate removal without anesthesia. None were removed prematurely. One child required subsequent endoscopic incision of a distal ureteral stricture (balloon dilatation at time of initial procedure). No other significant changes were noted on postoperative imaging.

Conclusion: The endoscopic treatment of proximal collecting system calculi in children appears to be safe, effective, and feasible. Significant postoperative morbidity is related to active balloon dilatation of the distal ureter. The role of ureteroscopy in the treatment of upper tract calculi in children needs further investigation.

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URETEROPYELOSCOPY AND HOLMIUM LASER LITHOTRIPSY FOR UPPER TRACT CALCULI IN CHILDREN

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Background: Shock wave lithotripsy (SWL) is considered first line therapy for upper urinary tract calculi in children. This is in part due to the limited experience with retrograde ureteroscopy (UPS) in children, the historical lack of small caliber ureteroscopes, and the danger or iatrogenic ureteral injury from orifice dilatation. We utilized a staged approach with pre-stenting of small caliber ureteral orifices to allow passive ureteral dilatation and subsequent ureteroscopy with holmium lithotripsy.

Methods: 26 stones in 18 children were treated during an 18 month period from 1997 to 1999. Ages ranged from 3-17 years. 14 patients had solitary stones and 4 multiple. Stones were located in the ureter in 8 patients, calyces in 11, and renal pelvis in 7. Prepubertal children underwent initial stent placement. After a waiting period of 7-10 days to allow stent-induced passive ureteral dilatation, a ureteroscopy procedure was performed using a 7.5 F flexible ureteroscope in conjunction with the Holmium laser. Postpubertal patients underwent initial UPS with pre-stenting reserved for cystoscopically determined small caliber ureteral orifices or difficult access.

Results: All prepubertal patients (9/9) were pre-stented and underwent successful ureteral entry at staged UPS; and none required balloon-dilatation. Of 9 postpubertal patients, 6 were pre-stented to facilitate upper tract access. 3 postpubertal patients underwent primary UPS. Stone treatment success was defined as lack of residual fragments >2 mm. in size on postoperative plain film or spiral CT. Of 26 stones, 3 passed spontaneously after pre-stenting. 20/23 (87%) of the remaining stones were successfully treated with a single ureteroscopy. Two of these three patients underwent repeat successful ureteroscopy yielding an overall success rate of 96%. Complications were minor, and there was no evidence of ureteral strictures at short-term follow-up.

Conclusion: Pre-stenting permits successful ureteral orifice entry at staged ureteroscopy even in the smallest children and infants. Balloon dilation of the ureteral orifice can be avoided in most children. Ureteroscopy and Holmium lithotripsy is effective in children for the treatment of upper tract stones and should be considered as an alternative to shock wave lithotripsy in experienced hands.

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HYPERCALCIURIA AND STONE RECURRANCE IN PEDIATRIC UROLITHIASIS

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Background: To date, the recurrence of stone disease in children has been seldom studied, particularly in regard to non-struvite stones and hypercalciuria. The large number of stone patients seen and treated at our institution allowed us to review those with hypercalciuria to see if there was a risk factor for long term recurrence of their stone disease.

Methods: Forty four children with documented hypercalciuria and calcium oxalate stones were identified in our patient population. Seven of these patients had underlying structural abnormalities, but all 44 children were otherwise metabolically normal.
Twenty nine patients could be completely evaluated as to long term followup and recurrence of their stone disease.  

Results: Nine of the 29 evaluable children (31%) had recurrence of their stone disease. There were 3 females and 6 males in this group with recurrent stones. Time to recurrence varied from 1 year to 15 years for an average of 7.2 years until the first stone recurrence. No patients were on specific treatment for their stone disease at the time of recurrence, although all had been counselled as to general dietary and fluid measurements to try to lower the chance of recurrent stones.

Conclusion: A child with calcium oxalate stones with or without underlying structural abnormalities appears to be at increased risk for recurrent stones if hypercalcuria is found to be present on metabolic evaluation. The recurrence rate appears to be somewhere in the range of 31% and could prove to be higher as many children had recurrent stones several years after their initial presenting episode.

LONG-TERM FOLLOW-UP OF ENDOSCOPIC INCISION OF URETEROCELES: INTRAVESICAL VERSUS EXTRAVESICAL

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Background: Endoscopic incision of a ureterocele now presents a standard treatment option in the modern management of ureteroceles. In 1993 our institutions reported their experience with endoscopic incision as initial therapy for ureteroceles in 51 children. These children had a minimum post operative follow-up of at least 1-year and only 27% required further surgery. To assess the long-term efficacy of this treatment modality we re-evaluated the outcome of these patients.

Methods: Forty-four of the original 51 patients had sufficient medical records for analysis. In 7 patients no extended follow-up was available excluding them from further analysis. Parameters reviewed included the patient’s age at surgery, position of the ureterocele (intravesical vs. extravesical), association with a duplex system, pre and post-operative reflux, function of upper pole, and the need for additional surgical procedures.

Results: The average age at the initial surgery was 1.9 years (standard deviation (SD)=3.7 years) with an average follow-up of 6.2 years (SD= 3.6 years). 22 patients had intravesical ureteroceles and 22 had extravesical ureteroceles, 31 had a ureterocele associated with a duplex collecting system while 13 had a single system ureterocele. 10 (77%) of the ureteroceles associated with a single system were intravesical while only 12 (39%) of the ureteroceles associated with a duplex system were intravesical. Of the 18 patients requiring a secondary procedure 14 had an extravesical ureterocele and 16 had duplex systems. 2 patients with a single system extravesical ureterocele underwent a secondary surgery. The average time to the secondary procedure after the initial incision was 1.4 years (SD=1.8). Secondary procedures included 13 patients undergoing ureteral reimplantation, 7 undergoing upper pole partial nephrectomy, 3 total nephroureterectomies, 3 bladder neck reconstructions, and 1 lower pole pyeloplasty. Only 1 child required surgical intervention following a secondary procedure. This child underwent a cystoscopic urethral incision of a partial ureterocele remnant. The only operations performed in the patients with intravesical ureteroceles were reimplantations and 1 upper pole nephrectomy performed at the time of a lower pole pyeloplasty. 69% of patients known to have no preoperative reflux developed reflux following endoscopic incision (36% from intravesical and 64% from extravesical). Of these patients 45% spontaneously resolved their reflux while another 45% required reim-plantation. Reflux persisted at the time of last follow-up in 10%. Of 22 patients with known function of the upper pole, 13 had intravesical and 9 had extravesical ureteroceles. All 9 patients without function of the upper pole had an associated extravesical ureterocele.

Conclusions: With extended follow-up we confirm the role of endoscopic incision in the primary management of ureteroceles previously reported by our institutions. Of note, the percentage of patients requiring secondary surgery after endoscopic incision increased from our original report of 27% to 41%. Only 18% with an intravesical ureterocele required a subsequent procedure compared to 64% of those with an extravesical ureterocele. The reduction in size of the obstructed ureter following primary endoscopic decompression facilitated successful ureteral reimplantation in those requiring a secondary procedure.

NATURAL HISTORY OF REFLUX IN PATIENTS WITH URETEROCELES

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Background: Much debate continues about the appropriate initial surgical management of patients with ureteroceles. Factors that influence treatment include the nature of the ureterocele, function of the involved segments and the presence of reflux. We reviewed our recent experience with ureteroceles concentrating on the natural history of associated reflux.

Methods: We retrospectively reviewed our last 75 patients with ureteroceles. As expected, most occurred in females (58:17) and duplicated systems (69:6). Initial presentation was infection in 39 patients, antenatal diagnosis in 33, prolapse in 2 and incontinence in 1. Patients with antenatal diagnosis were all evaluated in the first two months of life, and the others were evaluated at a mean age of 3.5 years (range 1month to 16 years). Function above the ureterocele was considered good in 17 upper pole or single systems and was decreased to absent in 61 units. Lower pole or contra-lateral impairment was relatively rare (12). Vesico-ureteral reflux was common occurring in 45 units (lower pole -29, upper pole-7, contra-lateral -9) and 35 of 75 patients (47%). Ipsilateral reflux was virtually always severe (≥ Gr III); any low-grade reflux was usually noted contra-laterally. Treatment included an upper tract approach in 37 units, endoscopic incision in 30, open bladder repair in 6 and observation in 2.

Results: Follow-up is available for 74 of 75 patients. In terms of the fate of pre-existing reflux, 5 patients underwent open bladder repair and one is being observed. Of the remaining 29 patients, decompression of the ureterocele was achieved by endoscopic incision (16) or with an upper tract approach (13), usually heminephrectomy. Regardless of management, reflux persisted in 19 units (18 patients), resolved in 11 units and improved in 3. New reflux after decompression occurred in 12 units (11 patients). Most involved the upper pole (8) after endoscopic incision although new lower pole or contra-lateral reflux was noted (4). After endoscopic incision among patients without initial reflux, upper pole reflux was created in 8 of 18 patients. Upper pole hemi-nephrectomy resulted in new lower pole or contra-lateral reflux in 4 of 18. We have not found subsequent resolution of any reflux to an upper pole system after ureterocele incision. In fact, only one of 28 patients with any new or persistent reflux after effective decompression of the ureterocele has shown late resolution despite being followed up to 5 years (mean 2.2 years).

Conclusions: New or persistent reflux after ureterocele decompression very rarely resolves. Consequently, patients with such
reflux should be treated surgically or eventually followed off daily antibiotics; numerous yearly voiding studies should be avoided. Any ureterocele decompression in the setting of reflux should probably be recognized as the first step of a staged repair. Perhaps, more initial consideration of complete bladder repair is warranted.

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ENDOSCOPIC PUNCTURE OF URETEROCELE AS MINIMAL INVASIVE AND LONG-TERM EFFECTIVE PROCEDURE IN CHILDREN

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Background: Over the past years the surgical approach to ureterocele has evolved from major surgery to minimally invasive endoscopic treatment. We have retrospectively evaluated long-term results of endoscopic puncture of ureterocele and its long-term effectiveness and applicability in children.

Methods: Over the past 8 years 34 patients (20 female, 14 male) were treated with primary endoscopic puncture of ureterocele. Mean age of the patients was 1.1 years. 80% of the children were below the age of 6 months. Mean follow up was 6.1 years. Intravenous ultrasound detected ureterocele in 5 (12%) patients, fetal hydronephrosis leading to the postnatal diagnosis in 13 (38%) and 17 (46%) children presented with symptoms of urinary tract infection (UTI). The ureteroceles presented as a part of renal duplication in 31 patients (91%), 3 (9%) in a single system and 1 child had bilateral ureterocele. Intravesical ureterocele existed in 20 (58%) children and ectopic, protruding into the bladder neck or urethra, in 14 (42%). Very poorly functioning upper pole moiety presented in 26 (75%) of the cases and non-functioning upper poles in 5 (14%). 20 out of 34 children (58%) had vesico-urethal reflux (VUR) to the lower moiety, either to the ipsi (60%) or contralateral kidney (40%). A cold knife incision was carried out in 4 (11.7%) puncture by Bugbee electrode F3 in 20 (58%) and F3 ureteral catheter stylet was utilized in the remaining 10 patients (30.3%). The puncture is done high on the ureterocele to avoid reobstruction at the bladder outlet by its prolapse.

Results: Complete decompression of ureterocele was observed in 32 out of 34 patients (94%) (p<0.05). 2 patients required secondary puncture 2 years following the primary procedure and do well. Upper pole moiety function improved postoperatively in two infants and remained stable in all 32 patients, no patient presented with deterioration of the renal function. 6 out of 20 (30%) who had VUR to the lower pole required surgery. 3 underwent ureteric reimplantation and another 3, submucosal teflon injection. Additional 6/17 (17.6%) patients developed VUR to the upper moiety after the procedure. 3 after cold knife incision and 3 after simple puncture. In 2, submucosal teflon injection solved the VUR and the remaining 4 patients were maintained on prophylactic antibiotics. In one child the reflux resolved spontaneously and none of them presented with UTI. In two cases with initially non function upper pole moiety partial nephrectomy was done due to symptomatic UTI in spite of complete collapse of the ureterocele, one and two years following the initial puncture. No difference was observed in the reoperation rate between the patients with ectopic versus intravesical ureterocele (p>0.05).

Conclusion: In contradiction to recent criticism we found that endoscopic puncture of ureterocele presents an easily performed procedure which allows the release of obstructive ureters. Coexisting reflux or its appearance after the procedure, can be treated by ureteric reimplantation or teflon injection.

SYMPOTHOMATIC URETEROPELVIC JUNCTION OBSTRUCTION IN CHILDREN IN THE ERA OF PRENATAL SONOGRAPHY—IS THERE A HIGHER INCIDENCE OF CROSSING VESSELS?

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Background: Due to the widespread availability and use of prenatal ultrasound screening, the majority of children with ureteropelvic junction obstruction (UPJO) now present at birth with hydronephrosis. Prior studies have suggested that prenatally diagnosed UPJO is rarely caused by obstructive lower pole crossing vessels. The likelihood of finding crossing vessels in pediatric patients with UPJO has clinical importance, as it may impact the operative approach (endoscopic vs. laparoscopic vs. open pyeloplasty). To determine if the incidence of crossing vessels has changed in children presenting with symptomatic UPJO since the introduction of widespread prenatal screening, we reviewed the etiology of obstruction in older children that underwent pyeloplasty for UPJO.

Methods: Medical records were reviewed for all patients that underwent pyeloplasty for UPJO since 1986. Guidelines for inclusion were: patient age > 3 years; flank pain +/- nausea, UTI or hematuria as the presenting symptom; renal scan and/or IVP demonstrating significant obstruction; and no history of prenatal hydronephrosis. Operative notes were reviewed to determine the etiology of UPJO. Open pyeloplasty was performed in every patient.

Results: Thirty-three of 157 pyeloplasties met the criteria for inclusion. Average patient age was 7.3 years (range 3.5-17.5 yrs), with 23 males and 10 females. Presenting symptoms included intermittent flank/abdominal pain in 28 (85%), febrile UTI in 3 (9%) and hematuria in 2 pts (6%). In 19/33 patients (58%) the attending surgeon felt that lower pole vessels contributed to the UPJO, and the UPJ was moved anterior to the vessels. This represents a significant increase in the incidence of crossing vessels compared to historical series of UPJO prior to the wide use of prenatal sonography (11%); Hoffer, Lebowitz, Radiology, 1985). This is also a much higher incidence than found in the asymptomatic or prenatally diagnosed patients operated on at our institution during the same era, with only 14/124 (11%) having crossing vessels. Additional etiologies of UPJO in our study population included stenotic segment in 5 (21%), ureteral tortuosity, fibroepithelial polyp, and periureteral fibrosis in 2 each (6%), and high ureteral insertion in the pelvis in one patient (3%). In the 28 patients that presented with pain, 19/28 (68%) had crossing vessels. These patients also had a longer duration of symptoms before evaluation, with 17/28 experiencing episodic pain for over one year. All patients had postoperative renal scans demonstrating no obstruction and have remained asymptomatic since surgery.

Conclusion: The incidence of lower pole crossing vessels as the etiology of UPJO has increased in children presenting with symptoms since the introduction of prenatal ultrasound screening. Potential explanations are: i) that crossing vessels do not cause hydronephrosis inureto, or ii) that a greater percentage of patients with intrinsic UPJO now undergo early repair due to prenatal screening. This higher incidence of crossing vessels as the etiology of symptomatic obstruction in older children may impact treatment decisions regarding surgical approach. Because of the high incidence of lower pole vessels in children presenting with pain (68%), and the excellent results with open pyeloplasty in this group, we recommend open pyeloplasty in this patient population.
THE LONG TERM FOLLOW-UP OF NEWBORN HYDRONEPHROSIS INITIALLY MANAGED NON-OPERATIVELY

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Background: It became clear in the last decade that hydronephrosis in the newborn does not necessarily represent obstruction and may improve with time. To better define its natural history, we performed long-term follow-up study of infants with this condition.

Clinical Material: 104 newborns with antenatally diagnosed primary unilateral grade 3-4 hydronephrosis were followed nonoperatively unless renal deterioration occurred whereupon pyeloplasty was performed. Results: All 23 infants (22%) who showed either progressive hydronephrosis or a reduction in differential renal function and required pyeloplasty were <18 months of age. Differential GFR returned to pre-deterioration levels and higher in all kidneys after surgery. Of 81 infants followed nonoperatively, 48 were followed long term (mean 78 months) and hydronephrosis either resolved (69%) or improved (31%). Mean time to maximum US improvement was 2.5 years. In those 76% with initial differential function >40%, final function averaged 49%. Initial differential function was less than 40% (mean 23%) in 24% of cases, and within 18 months (mean) differential function reached 47% (mean). The initial T1/2 time in nonoperative patients was >30 in 37%, 20-30 in 21% and <20 in 42%. Final T1/2 time was >30 in 18%, 20-30 in 17% and <20 in 55%. Before pyeloplasty T1/2 time was >30 in 95% and 20-30 in 5%; postoperatively the values were similar to non-operative patients: T1/2 time >30 in 10%, 20-30 in 25% and <20 in 65%.

Conclusion: Natural history suggests that unilateral newborn hydronephrosis is relatively benign. Dilation and function improve with time. Close follow-up is necessary to identify <25% of infants with obstruction who require prompt pyeloplasty to prevent loss of renal function. Standard tests for assessing obstruction in older patients are invalid in infants: a prolonged T1/2 time and/or high grade hydronephrosis are neither indicators of obstruction nor indications for surgery. Non-operative management with close followup during the first 2 years is the safe and recommended approach for these children.

RENAI‘PELVIS HISTOPATHOLOGY CORRELATES WITH RADILOGIC OUTCOME FOLLOWING PYELOPLASTY IN CHILDREN WITH UPJ OBSTRUCTION

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Background: The clinical management of children post-pyeloplasty with persistent hydronephrosis (HN) by ultrasonography(US) or prolonged 1½ drainage by Well Tempered Renography (WTR) is not well structured. Reasons for unresolved hydronephrosis include irreversible pathologic changes in the proximal collecting system, transient obstruction due to edema at the site of repair, and persistent obstruction due to failed pyeloplasty. To help in the differentiation of these possibilities, this study correlated various histopathologic features of the excised renal pelvic specimen to radiologic outcome following pyeloplasty.

Methods: Of 220 children that underwent pyeloplasty between 1988-1996 for isolated ureteropelvic junction (UPJ) obstruction, 41 children (42 kidneys) on retrospective review had adequate postoperative radiographic studies (US and/or WTR), and histologic specimens. Prenatal hydronephrosis was the diagnosis in 36/41 patients. The median age at time of pyeloplasty was 3.3 months. Median follow-up was 19.7 months (range 3 months to 7 yrs) with intervals at 3, 6, 9, 12 months and 2 years. Radiologic improvement in HN was defined as a decrease in ≥ 1 grade (Society for Fetal Urology grading system). Improvement in a WTR was defined as a decrease in drainage time (t½ >5 min or 20%) or non-observed curve. Histologic features of the muscularis propria (MP) in the renal pelvic specimen (μm thickness, % surface area collagen and elastin content / distribution) were correlated with the radiographic time line.

Results:

<table>
<thead>
<tr>
<th>Post Pyeloplasty Radiologic Improvement</th>
<th>follow-up</th>
<th>based on US</th>
<th>based on WTR</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>8/26 (31%)</td>
<td>9/15 (60%)</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>17/30 (57%)</td>
<td>14/18 (78%)</td>
<td></td>
</tr>
<tr>
<td>9 months</td>
<td>22/26 (80%)</td>
<td>22/26 (85%)</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>26/27 (96%)</td>
<td>25/28 (89%)</td>
<td></td>
</tr>
<tr>
<td>2 years</td>
<td>29/30 (97%)</td>
<td>25/27 (93%)</td>
<td></td>
</tr>
</tbody>
</table>

Radiologic Improvement via MP Thickness

<table>
<thead>
<tr>
<th>follow-up</th>
<th>&lt;250 um</th>
<th>&gt;250 um</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months</td>
<td>9/9 (100%)</td>
<td>6/21 (29%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6 months</td>
<td>10/10 (100%)</td>
<td>12/24 (50%)</td>
<td>&lt;.005</td>
</tr>
<tr>
<td>9 months</td>
<td>11/11 (100%)</td>
<td>18/23 (78%)</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>11/11 (100%)</td>
<td>19/23 (83%)</td>
<td></td>
</tr>
<tr>
<td>2 years</td>
<td>12/12 (100%)</td>
<td>20/21 (95%)</td>
<td></td>
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</tbody>
</table>

Of the various histologic measures, only MP thickness significantly correlated with radiologic improvement (n=39). At 3 months, 15/30 (50%) patients with radiologic improvement had a mean MP thickness of 240±33.0 (mean ± S.E.M.) while the remaining 15 patients without improve had a mean MP thickness of 377±16.3 (p<.001). At 6 months, 22/34 (64.7%) patients with radiologic improvement had a mean MP thickness of 255±25.7 while the remaining 12 patients without improve had a mean MP thickness of 376±18.7 (p<.001). Two patients that did not have radiologic improvement and underwent reoperation at 9 months and 20 months (MP thickness were 397μm and 416μm respectively). Average MP thickness of the age matched control was 97 μm (n=9). Both % collagen and elastin did not correlate with improvement of hydronephrosis and/or drainage time at any study time point.

Conclusions: MP thickness of the renal pelvis was found to correlate significantly with the radiographic improvement during clinical follow-up i.e. specimens with MP thickness <250μm show faster improvement in US and/or WTR than thicker specimens. Additionally, we have shown a time line to expect radiologic improvement in post-pyeloplasty children. These findings can be clinically used post-pyeloplasty to guide pediatric urologists to differentiate children with non improved radiologic studies with ultimate good outcome from those requiring intervention for persistent obstructive hydronephrosis.
RENAL EXPRESSION OF HB-EGF INHIBITS MECHANICAL STRETCH-INDUCED APOPTOSIS IN COLLECTING DUCT CELLS

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Introduction: We previously have demonstrated that in vivo, ureteral obstruction induces a transient increase in heparin-binding epidermal growth factor-like growth factor (HB-EGF) gene expression in the obstructed kidney and that in vitro, mechanical stretch (such as that seen in hydropneumotropic distention) induces a similar but more sustained increase in HB-EGF expression. These findings indicate that obstruction results in regional and cell-specific regulation of the HB-EGF gene in the kidney, suggesting a functional role for this growth factor in renal pathology. Moreover, recent studies have suggested that the expression of HB-EGF may serve a protective role by preventing cell death. In this study, we investigated whether the expression of HB-EGF in renal collecting duct cells can inhibit stretch-induced apoptosis.

Methods: Renal collecting duct cells were engineered to express large amounts of human proHB-EGF, the soluble HB-EGF precursor, by transfection of the proHB-EGF gene cloned behind a strong promoter, followed by stable selection of transfected cells with the antibiotic, G418. RT-PCR and western blot analysis was used to identify clones expressing high levels of HB-EGF. Transfected and untransfected (control) cells were grown on collagen coated, silicon elastomer-bottomed culture plates and were subjected to continuous cycles of stretch/relaxation of high frequency and magnitude (extreme stretch) to induce cell death. Apoptosis was then assessed by the presence of nucleosomal DNA laddering. To determine whether the inhibition of apoptosis was directly attributed to HB-EGF expression, transfected cells were stretched in the presence of CRM197, a specific inhibitor of human, but not rat HB-EGF.

Results: We observed that “extreme” stretch induced apoptosis in untransfected collecting duct cells. In contrast, cells that stably expressed HB-EGF did not undergo apoptosis in response to “extreme” stretch. However, in the presence of CRM197, the HB-EGF transfected cells demonstrated DNA laddering following stretch, suggesting that the expression of HB-EGF was directly involved in preventing apoptosis.

Conclusions: The above findings suggest that the expression of HB-EGF is cytoprotective by preventing apoptosis in renal collecting duct cells. Together with the results of previous studies, we suggest that HB-EGF expression in renal epithelial cells is induced in response to the mechanical stretch caused by hydropneumotropic distention from renal obstruction. This response may serve to protect the kidney from injury induced by obstruction. However, in vivo, this response appears to be transient with continued obstruction. Further studies in the regulation of renal HB-EGF expression will help to identify cellular mechanisms that can protect the kidney from apoptosis induced by obstruction.

THE EFFECT OF A BRADYKININ ANTAGONIST (HOE140) ON RENAL PARENCYHMAL INJURY FOLLOWING UNILATERAL URETERAL OBSTRUCTION

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Background: The renin-Angiotensin System (RAS) and the Kinin-Kallikrein System (KKS) are linked such that a single enzyme, angiotensin converting enzyme (ACE), increases the activity of the RAS while simultaneously decreasing the activity of the KKS. Both systems are altered following renal parenchymal injury such as unilateral ureteral obstruction (UUO). For reasons not completely understood, the renal expression of the kininase enzyme kallikrein has previously been shown to decrease after renal injury. Mice with a known mutation in the angiotensin type 2 receptor (AT2) are known to demonstrate a higher susceptibility to renal injury following UUO. This study evaluates the effects of a bradykinin antagonist, HOE140, on the KKS following 3 days of UUO in a mouse model. Using a known tissue marker for renal parenchymal fibrosis (TGF-β) we also investigate the possible renoprotective effects of HOE140 following UUO.

Methods: AT2 mice (n=18) and wild type mice (n=14) were grouped into 4 equal treatment arms: 1) no intervention, 2) treatment with HOE140 only, 3) creation of UUO only, 4) creation of UUO and treatment with HOE140. Animals with UUO were harvested 3 days following obstruction and renal mRNA was analyzed for TGF-β (a marker of fibrosis) and kallikrein expression by Northern blots.

Results: HOE140 alone had a minimal effect on TGF-β levels. UUO alone caused drastic elevations in TGF-β. This effect was greatly blunted by the concomitant treatment with HOE140, to a greater extent in the AT2 mice. Kallikrein levels increased in the AT2 but not in the wild type animals when treated with HOE140 in the absence of UUO. All mice showed striking decreases in Kallikrein after UUO and there was no difference between the AT2 and wild mice. Treatment with HOE140 partially reversed this effect to an equal extent in both groups.

Conclusion: Antagonism of bradykinin ameliorates elevations of TGF-β, a marker of renal parenchymal fibrosis, following UUO. In addition, bradykinin antagonism lessens the decrease in kallikrein activity induced by UUO. Injury induced by UUO is mediated not only through the RAS but the KKS as well. Lessening the activity of the KKS in the setting of urinary tract obstruction may offer protective benefits to the kidney.

RENAL FUNCTION AND MORPHOLOGY IN EXPERIMENTAL UNILATERAL HYDRONEPHROSIS: ARE EARLY MRI MORPHOLOGY OR RENOGRAPHY PREDICTORS OF THE OUTCOME?


Background: Congenital hydronephrosis has previously been categorized on the basis of differential uptake on renograms, pelvic size and length of the contralateral kidneys. The purpose of this study was to follow the spontaneous course of neonatally induced unilateral hydronephrosis in pigs and to establish if early functional or morphological evaluation of the obstructed kidney could predict the outcome.

Methods: In 12 piglets a unilateral partial ureteropelvic obstruction was created at 2 days of age (a.m. Ulm and Miller) and 9 piglets were sham operated. Renal function was assessed using 99mTc-DTPA differential uptake on renography, and from the plasma clearance of 99mTc-DTPA GFR was determined at 4, 12, and 24 weeks of age. In parallel kidney morphological was studied using MRI.

Results: At 4 weeks all obstructed kidneys had severe hydronephrosis. Two of 6 obstructed kidneys with a functional share (FS) > 40 % deteriorated from a FS of 44 % and 40 % at 4 weeks to a FS of 17 % and 22 %, respectively, at 24 weeks of age. Four of 6 obstructed kidneys with an FS below 40 % at 4 weeks improved to an FS above 40 % at 24 weeks of age. Single kidney GFR (SKGFR) of the obstructed kidneys at 4 weeks did not correlate with SKGFR at 12 or 24 weeks, but SKGFR at 12 weeks correlated with SKGFR at 24 weeks (r² = 0.8140, p < 0.001). Relative kidney volume reflects the degree of hydronephrosis. Relative kidney volume.
volume of the obstructed kidney did not correlate to FS at any age. No correlation was observed between contralateral kidney length and FS of the obstructed kidney at any age.

**Conclusion:** The individual functional course of the obstructed kidney was neither predicted by early renographic evaluation, or initial SKGFR, or the degree of hydropnephrosis or the length of the contralateral kidney. However, SKGFR of the obstructed kidney at 12 weeks predicted the functional outcome at 24 weeks of age. Our results suggest that early evaluation of kidney function and kidney size do not predict the outcome in neonatally induced unilateral severe partial obstruction in pigs.

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COMPARISON OF SURGICAL (UOO) VERSUS CONGENITAL OBSTRUCTION OF THE URINARY TRACT IN AN ANIMAL MODEL: ARE THEY THE SAME?

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**Background:** The study of congenital obstruction (CO) of the urinary tract has long been hampered by the lack of an adequate animal model. Mice with a null mutation of the angiotensin type 2 receptor (AT2) are known to have congenital obstruction of the urinary tract with a penetrance and phenotypic expression similar to humans. Many of these animals have significant hydropnephrosis with parenchymal thinning and contralateral renal hypertrophy. The changes associated with surgically created unilateral ureteral obstruction (UUO) are also well known in both wild type and AT2 mice and this study compares renal parenchymal changes of surgical UUO to those of congenital urinary tract obstruction.

**Methods:** AT2 knockout mice with CO at the ureterovesical junction were compared to wild type controls at birth (d0), 3 weeks, and 8 weeks of age. In addition, animals with CO were compared to wild type animals with 1 week of UUO at the UVJ at ages 3 and 8 weeks. There were 6 animals in each group for a total of 48 animals. Obstructed and control kidneys were harvested, fixed in 4% buffered paraformaldehyde, embedded in paraffin and sectioned. The specimens were stained with periodic acid Schiff, and immunohistochemical staining using anti-smooth muscle actin (SMA), F4/80 (macrophage), and Masson trichrome (fibrosis) was performed. Glomerular size and density were measured planimetrically. Results were quantified and statistically compared using the Fisher’s PLSD test.

**Results:** At birth, animals with CO had a decrease in glomerular size compared to controls. At 3 and 8 weeks of age, however, these animals showed appropriate glomerular maturation and growth although glomerular size remained smaller than controls. Glomerular size in animals with 1 week of UUO showed no change at any point compared to controls. There was no difference in glomerular density among any group at any point in time. Smooth muscle activity was greater in CO animals than in controls at birth but showed minimal progression with time. Animals with UUO showed greater-SMA activity than either AT2 mice or controls at all ages. Relative to controls, there was no increase in macrophage number at any age in animals with CO compared to a very large increase in the number of macrophages in animals with UUO. There was minimal staining for interstitial fibrosis in the CO animals and this did not progress with age. Animals with UUO showed moderate interstitial fibrosis at both 3 and 8 weeks following one week of obstruction.

**Conclusion:** Renal parenchymal injury clearly occurs in animals with congenital obstruction of the urinary tract, however these changes occur to a much lesser degree and appear to progress at a much slower rate than in animals with surgical UUO. This fact may certainly relate to a variable degree of obstruction in the CO population. Maldevelopment of the kidney in animals with congenital obstruction, however, appears to be preprogrammed during embryonic development and shows a minimal inflammatory component as opposed to surgical UUO which results in a significant inflammatory response with subsequent interstitial fibrosis. This study supports the fact that surgical obstruction and resultant parenchymal damage is a poor model of congenital obstruction. Future efforts will focus on the embryologic aberrations that occur in these animals with congenital anomalies of the kidney and urinary tract.

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PRIMARY OBSTRUCTIVE MEGAUORETER MANAGED BY URETERIC STENTING: EXPERIENCE AND LONG-TERM OUTCOME

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**Background:** The majority of infants with an antenatally diagnosed megaureter do not require surgery, however, a few develop symptoms or have deteriorating renal function and need surgical correction. The risk of creating a neuropathic bladder in infants, following ureteric reimplantation, has led us to temporarily overcome the obstruction using a ureteric stent. The aim of this study is to evaluate our experience using a ureteric stent in children with an obstructed megaureter.

**Methods:** This study is a retrospective review of patient’s notes and a prospective blinded review of imaging. All patients with an obstructive megaureter treated with a double J ureteric stent between 1991 and 1997, from one institution, were included.

**Results:** Thirteen patients were identified, 12 were diagnosed antenatally and 1 following a urinary tract infection. In 9 the megaureter was bilateral and in 4 children unilateral. The indications for open insertion of the double J stent were: urinary tract infection in 6; increasing hydropnephrosis in 4 and reduced renal function in 4. The mean age of insertion was 6.6 months (range 1–14.5), the stent was kept in place for 10.9 months (range 6–19). The mean follow up is 39 months (range 13–81). Three children developed a urinary tract infection with the stent in place, all were successfully treated with antibiotics alone. Following stent removal 7 have required no further ureteric surgery, 5 have subsequently needed ureteric reimplantation. Two patients had large capacity bladders with inadequate emptying and have undergone a Mitrofanoff procedure. Those patients who required ureteric reimplantation could not be predicted pre-stent insertion by features on MAG 3 renography, ultrasound or MUG. No child had a permanent drop in renal function.

**Conclusions:** The majority of infants with primary obstructive megaureter can be managed non-operatively. Infants, who fail medical management, can be successfully and safely treated with the temporary insertion of a ureteric stent. Following the removal of the stent over half the children require no further ureteric surgery.

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URETEROSCOPIC ENDOPYELETOMY FOR RECURRENT UPJ OBSTRUCTION IN CHILDREN

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**Background:** Minimally invasive procedures are commonly used for recurrent ureteropelvic junction obstruction (UPJ) after failed open pyeloplasty. Options include antegrade and retrograde (Accucise) endopyelotomy and retrograde balloon dilatation. How-
ever, these approaches have significant drawbacks. Antegrade endopyelotomy requires a percutaneous nephrostomy with its associated morbidity and costs. Retrograde Accucise endopyelotomy provides a fixed incision length, which may not meet the needs of each clinical situation. Balloon dilatation alone has a high failure rate. The option of retrograde ureteroscopic endopyelotomy offers distinct advantages to these three approaches by allowing a customized incision under direct visualization. The development of small caliber ureteroscopes and endolumenal ultrasound now allows for increased safety by minimizing the risk of stricture and bleeding from adjacent vessels. The technique and our experience to date are reviewed to assess the feasibility and efficacy of this procedure in children.

Methods: Three children (aged 3, 4 and 16 years) have undergone retrograde ureteroscopic endopyelotomy between 9 and 72 months after an initial open pyeloplasty for UPJ failed. Retrograde balloon dilatation was performed unsuccessfully in 2 children prior to endopyelotomy. The technique involves a 6.9 Fr rigid or 7.5 Fr flexible ureteroscope in combination with endolumenal ultrasound to visualize the UPJ and the surrounding tissues in the same setting. Transmural incision of the stenotic UPJ is performed with electrocautery and/or the Holmium: YAG laser under direct vision. A ureteral stent is left indwelling for 6 weeks and a Foley catheter is left overnight; patients are observed in the hospital for 23 hours. Follow-up to date has been 12, 16 and 29 months respectively.

Results: Ureteroscopic endopyelotomy with endolumenal ultrasound guidance has been successful in all three patients. No intraoperative or postoperative complications have developed and all patients have been fit for discharge the day after surgery. Both ultrasound and diuretic renal scan have demonstrated resolution of the recurrent UPJ in each patient.

Conclusions: Ureteroscopic endopyelotomy with endolumenal ultrasound guidance is technically possible in the pediatric population and has been uniformly successful in our hands to date. This approach allows for tailoring of the endopyelotomy incision for individual anatomy and success is possible despite a failed prior balloon dilatation. The procedure is associated with minimal morbidity and a short hospital stay, and does not require nephrotomy access. Ureteroscopic endopyelotomy is an easy, safe, and effective treatment option for recurrent UPJO in children after a failed pyeloplasty.

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LESSONS LEARNED FROM LASER WELDING AND FIBRIN GLUE PYELOPLASTIES IN AN IN VIVO CHRONIC PORCINE MODEL

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Introduction: In the past 20 years, laser technology has become of standard use for many clinical situations. Laser welding is a more recent application, and in urology it has been used mainly for hypospadias repair and vasovasostomy. The use of fibrin glue for tissue reapproximation is also an emerging application. Classically sutured anastomoses are associated with 10% restenosis rate. We hypothesized that laser welding or fibrin glue would result in a watertight anastomosis with minimal scarring, allowing for improved long term potency.

Purpose: Our objective was to evaluate laser welding (804 nm) using a 50% albumin solder mixed with indocyanine green and fibrin glue to perform spatulated dismembered pyeloplasties, and to compare these two techniques with a standard sutured anastomosis.

Methods: 41 swine weighing 10 Kg were included in this study. We performed 49 pyeloplasties using one of the 3 techniques (suture, laser, fibrin glue), and animals were separated into 4 groups. An acute group, where leak point pressure (LPP in cmH2O) was measured after performing a pyeloplasty and three chronic groups studied at 3 days, 10 days and 30 days. In the chronic groups, pyeloplasties were performed over an indwelling 4 french double J ureteral stent and at the end of each of these time points animals were euthanized and a pressure/flow study (P/F at 10cc/min in cmH2O) was done.

Results: In the acute studies laser welding (n=8) had a significantly better mean LPP (55.4 cmH2O) than sutured (n=5) with 17.3 cmH2O or fibrin glued (n=5) pyeloplasties with 3.5 cmH2O. In the chronic studies (3, 10, and 30 days), animals in the sutured pyeloplasties groups (n=5/time point) had no post-operative complications and all P/F studies had low P (<10 cmH2O) except for one animal at 10 days with P of 198 cmH2O. In the chronic laser groups, we observed 6 urinomas in 11 animals, 5 occurred in the first 6 animals and 1 in the last 5 animals we operated (3/7 animals at 3 days and 3/4 animals at 10 days). The improvement corresponds with complete control of antegrade and retrograde urine contamination and improved albumin solution application. We were able to perform P/F studies in 3 animals at 3 days and 1 animal at 10 days post laser pyeloplasty and all 4 pressures were in the unobstructed range. In the chronic fibrin glue groups, 3/9 animals in the 30 days group had urinomas and the other 2 had unobstructed P/F studies.

Conclusion: We have not demonstrated that laser welding using an albumin solder or fibrin glue is superior to classic sutured pyeloplasty. Fibrin glue does not appear to be appropriate to perform this type of repair in our in vivo animal model. Laser welding using a 50% albumin solder mixed with indocyanine green is technically challenging, and its success depends on many variables. Our first in vivo attempts were associated with urine leakage, but with technical improvement (control of urine output, bleeding, improved laser fiber and albumin application) our recent clinical outcome and functional results have improved.

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ULTRASONOGRAPHIC REEVALUATION OF A COHORT OF CHILDREN WITH PRENATALLY-DETECTED MULTICYSTIC DYSPLASTIC KIDNEY (MDK) AND EVALUATION OF FIRST DEGREE RELATIVES

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Background: We have previously reported the familial occurrence of unilateral Multicystic Dysplastic Kidney (MDK) in three families (Multicystic Dysplastic Kidney: An Inherited Anomaly? Belk R.A. et al. Urology Section, AAP Annual Meeting 1997). 8 affected individuals were found from a total of 24 family members
investigated with renal ultrasound scans. However, the familial nature of MDK in these families was a serendipitous discovery due to either a prenatally-detected MDK in a second sibling or clinically-presenting renal pathology in a relative. A systematic family-screening study was therefore undertaken to determine the prevalence of unilateral MDK, unilateral renal agenesis and other renal anomalies in the first degree relatives of a cohort of children with prenatally-detected MDK. A secondary aim of the study was to reevaluate the longer-term management of prenatally-detected MDK.

Methods: Detailed urinary tract ultrasonography was performed by a designated ultrasonographer for 112 individuals–27 children with prenatally-detected MDK and 85 asymptomatic first degree relatives. Height was recorded in 112 individuals and weight in 107. Blood pressure measurements were obtained in 26 index cases and 85 first degree relatives. Plasma creatinine levels were measured in 19 index cases and 78 first degree relatives. Including the 4 prenatally-diagnosed members of the previously-reported families gave 31 affected children in total. Ultrasonographic reevaluation of the index cases was performed at a mean of 6.7 years of age, ranging from 3 months to 12 years.

Results: Family Study: No case of unilateral MDK or unilateral renal agenesis was identified in any of the 85 first degree relatives. Other renal anomalies were detected in 3 relatives—one with a duplex kidney, one with medullary sponge kidney and one with a rotated kidney. For all relatives, values for height, weight, blood pressure and plasma creatinine were within the age-adjusted normal range. Children with unilateral MDK: Of the 31 cases, 4 children had undergone nephrectomy in infancy while 27 had been managed non-operatively. Values for height, weight, blood pressure and plasma creatinine were all within the age-adjusted normal range with the exception of one index case, managed conservatively, who had a slightly raised blood pressure. This was normal at follow-up. Of the 27 cases managed conservatively, 14 (52%) had undergone complete involution whereas 13 (48%) were still detectable on ultrasound imaging. There was no correlation between the age of the individual and the likelihood of involution of the MDK.

Conclusions: 1. Although some families show a familial occurrence, MDK is usually a sporadic anomaly. 2. The overall prevalence of significant renal anomalies in the families of children with prenatally-detected MDK is low and we suggest that screening of family members is not justified. Ultrasound screening of subsequent pregnancies should detect any familial cases of MDK. 3. The frequency of involution of MDKs is 50% at a mean age of 6.7 years. Involution does not occur at a steady or predictable rate. This study was funded by the Wellcome Trust.

LONG TERM RESULTS OF GENITOPLASTY FOR PENILE AGENESIS, DYSEGENESIS AND MICROPHALLIA

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Background: In recent years doubts have been cast on the appropriateness of sex reassignment of genetic males born with serious and potentially devastating penile abnormalities. Some recommend that gender assignment be delayed until the child reaches adulthood and is capable of choosing a gender.

Methods: We reviewed the records of 17 genetic males (46XY) with serious penile deficiency treated between January 1980 and December 1998. The abnormalities included micropenis, who failed to respond to testosterone (4), total penile agenesis (3), absent or diminutive phallus associated with bladder extrophy (4), rudimentary bifid phallus with cloacal extrophy (4), a repaired hypospadias in a micropenis where the crura and erectile tissue were absent (1), and one child with hemihallus (i.e. one crura). The treatments included sex reassignment and vaginal construction in 11, penoplasty in 2 and penile construction using abdominal pedicle skin flaps in 2 and forearm flaps in 2. All children were followed up between 3 months to 18 years. Evaluations by school psychiatrists were available in 4/6 phenotypic males.

Results: The surgical results were satisfactory in 10/11 children post vaginoplasty, one child developed vaginal stenosis. 4/11 are sexually active and are well adjusted. There were six phenotypic boys of whom 2 underwent penoplasty. One is isolated, dependent and lonely and his mother’s reaction is based on guilt about the ‘damaged child’. Older parents adopted the other child, he has significant psychological maturational deviation and confusion about his gender identity. The two boys with reconstructed phallices suffer from feelings of inadequacy and incompleteness. One of them has primitive views on sexuality and fantasizes about having a ‘better penis’.

Conclusion: It would appear that early gender reassignment with removal of the gonads provides a satisfactory long-term outcome. Although phalloplasty is technically feasible the surgical and psychological outcomes were unsatisfactory.

CORPITAL TISSUE FOR PENILE RECONSTRUCTION

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Background: The aim of phallic reconstruction is to achieve structurally and functionally normal genitalia. We have previously shown that human cavernosal smooth muscle and endothelial cells seeded on polymers would form tissue composed of corporal cells when implanted in vivo. However, corporal tissue structurally identical to the native corpus cavernosum could not be achieved, due to the type of polymers used. We developed a naturally derived acellular corporal tissue matrix that possesses the same architecture as native corpora. In this study, we explored the feasibility of developing corporal tissue, consisting of human cavernosal smooth muscle and endothelial cells in vivo, using the acellular corporal tissue matrices as a cell delivery vehicle.

Methods: Acellular corporal tissue matrices were derived from processed donor rabbit corpora, using cell lysis techniques. Primary human corpus cavernosal smooth muscle and endothelial cells, obtained from routine penile surgeries, were seeded on the acellular matrices at a concentration of 30 x 10^6 cells/ml and 3 x 10^6 cells/ml, respectively. A total of 60 tissue matrices seeded with cells and 20 control matrices without cells were implanted in the subcutaneous space of 20 athymic mice. An additional 36 acellular tissue matrices seeded with cells were grown in culture for 1, 2, 3 and 4 weeks. Scanning electron microscopy was performed to confirm cell attachments to the corporal tissue matrices. Mice were sacrificed at 3 days, 1, 2, 4, 6 and 8 weeks after implantation. Immunocytochemical and histochemical studies were performed using alpha-smooth muscle actin and Factor VIII antibodies.

Results: Scanning electron microscopic examination of the seeded cells in vitro demonstrated a uniform attachment on the sinusoidal walls within the corporal tissue matrix. The implanted corporal tissue matrices maintained the seeded cells on the sinusoidal wall and showed host cell infiltration 3 days after implantation. Formation and migration of neovascularization into the sinusoidal spaces was evident by 1 week after implantation. Increasing organization of smooth muscle and endothelial cells lining the sinusoidal wall was observed at 2 weeks and continued with time. The corporal tissue matrices were completely covered with the appropriate cell architecture 4 weeks after implantation. Immunocytochemical studies using alpha-actin and Factor VIII antibodies
confirmed the presence of the corporal smooth muscle and endothelial cells, both in vitro and in vivo, at all time points. There was no evidence of cellular organization in the control matrices.

**Conclusion:** This study demonstrated that human cavernosal smooth muscle and endothelial cells seeded on acellular corporal tissue matrices are able to form vascularized corporal structures in vivo. The use of these tissue matrices as cell delivery scaffolds allowed for the development of adequate constructs. The formation of corporal structures, similar to that of the native erectile tissue, may provide an additional armamentarium in the management of complex penile reconstructive challenges.

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**RESULTS OF RECONSTRUCTION OF CHILDREN WITH HIGH UROGENITAL SINUS**

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**Background:** A common channel for the urinary and genital tracts is a normal stage of fetal development. It is also a normal feature of the fully developed male fetus. Severe virilization of the female fetus can produce a urogenital sinus. The confluence of the vagina and urinary tract may be high i.e. above the external sphincter, or low. The length of the common channel may be more or less than 3cm, the former presenting a significant technical challenge. The surgical determinants are: the level of confluence (high or low), the number of vaginas (single or duplex), the length and capacity of the vagina and the mobility of the vagina, which is determined by the degree of adherence to the urethra and bladder neck.

**Method:** We reviewed the records of 24 children with high urogenital sinus treated between 1980 and 1999. 8 children were masculinized due to congenital adrenal hyperplasia and 16 were pure urogenital sinus without genital ambiguity and normal anorectal canal. The initial treatments prior to referral included intermittent catheterization in 2, vesicostomy in 2 and vaginostomy in 2. Three children had clitoroplasty, labioplasty and attempted vaginoplasty prior to referral. Each patient was evaluated by ultrasonography, genitography and endoscopy prior to surgical reconstruction. The surgical approaches included abdominoperineal pull through in 8, transpubic repair in 5, perineal and transstriginal in 2, and pre-anorectal-perineal (PAP) in 9. All children were in place in the lithotomy position with full access to the pelvis, abdomen and anorectal canal. 17/24 had additional abdominal procedures, including take down vaginostomy, or vesicostomy, uretrocystectomy with or without tapering.

**Results:** In general satisfactory exposure was achieved in all. The PAP approach provided the best exposure and the least morbidity. The abdominal exposure allowed for urinary tract reconstruction without changing the position or re-prep of the child. The surgical morbidity included 3 with vaginal stenosis, which were revised. One child who had multiple attempted repairs in the past developed a small urethral fistula, which healed after 6 weeks of catheter drainage. 4 children are emptying their bladder or continent reservoir by clean intermittent catheterization. Thus 8/24 encountered significant morbidity.

**Conclusion:** High urogenital sinus represents a surgical challenge, with vaginal mobilization being the most tedious part of the operation. The PAP approach provides direct access to the high confluence of the urogenital sinus. This is facilitated by retracting the rectum posteriorly with a Deaver retractor. The lithotomy position allowed for abdominal exploration and correction of associated abnormalities, and at present the PAP is our approach of choice.

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**INITIAL EXPERIENCE WITH THE TRANSURETHRAL SELF-DETACHABLE BALLOON SYSTEM FOR URINARY INCONTINENCE.**

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**Introduction:** The transurethral treatment of urinary incontinence with a detachable balloon system was introduced by Yoo, et al. in 1997 in an animal model. We describe our preliminary
experience with application of this device to ten patients with urinary incontinence due to intrinsic sphincter weakness.

Patients and Methods: Ten patients ranging in age from 7 to 36 years (mean = 15.6 yrs) were treated. There were eight males and two females. Eight patients (7M, 1F) had spina bifida. One of these males had previously undergone an unsuccessful Pippi-Salie procedure, and the other seven had no prior bladder neck surgery. One patient had neuropathic bladder secondary to an anterior spinal artery bleed and one female patient had cloacal extrophy. Treatment was performed on an outpatient basis, utilizing a Wolf offset lens nephroscope, either 10 or 15 Fr, depending upon urethral caliber. In all but the cloacal extrophy patient, 0.9 cc balloons were utilized. One patient required two treatments. Between two and eight balloons were placed (mean=5). The cloacal extrophy patient had two 0.2 cc balloons placed. In females the balloons were placed at the bladder neck. In males, balloons were placed in the posterior urethra at the level of the sphincter. Each patient underwent UDS within 6 weeks prior to balloon treatment. A follow-up assessment with UDS was carried out 1 month postop.

Results: Patients were assessed in terms of clinical improvement (Dry, Markedly improved (= dry for some entire days), Improved (= longer dry intervals) or Unchanged. The urodynamic parameters assessed included UPP (urethral resistance and functional length) and bladder capacity. Patients were grouped according to those with and those without prior Bladder neck surgery.

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There were no perioperative complications associated with the technique.

Conclusions: For patients with urinary incontinence due to intrinsic sphincter weakness who have had no prior bladder neck or urethral surgery, the self-detachable balloon system appears safe and promising as a minimally invasive surgical approach to produce continence. 75% of unoperated patients became dry or markedly improved post treatment. The technique was easiest and most successful in the female patient. It appears to be inapplicable to surgically reconstructed bladder necks.

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PLACENTAL ESTRADIOL: A PURPORTED ETIOLOGIC FACTOR OF HUMAN CRYPTORCHIDISM

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Background: The crucial involvement of estradiol in the etiology of experimental cryptorchidism has been well established since 1938. Estradiol injected into pregnant rodents induced either uni- or bilateral cryptorchidism in 75-100% of the male offspring, while concomitantly lowering significantly testicular testosterone and causing atrophy of Leydig cells due to an impaired gonadotropin secretion. An impaired secretion of gonadotropin was found also in cryptorchid boys. This had an impact on the development of Leydig cells resulting in insufficient testosterone secretion. It has been argued convincingly that the increasing incidence of reproductive abnormalities in the human male may be related to increased estrogen exposure in utero Consumption of estrogen by mothers during the first four months of pregnancy has been implicated in cryptorchidism. In the present study, we document the expression of estradiol in the syncytiotrophoblast of boys born with cryptorchidism compared to the placentas of boys and girls born with normal genitalia.

Methods: Biopsies of the newborn placentas were fixed in glutaraldehyde and embedded in Epon for immunohistological procedures. The genitalia of the newborn were examined immediately after birth. Those boys with either unilateral or bilateral cryptorchidism were reexamined after one year and followed until treatment. Seven boys in this study had cryptorchidism: six unilateral, one bilateral. Semi-thin histological sections of placental biopsies of these seven boys together with seven randomly selected normal male and seven female placentas were analyzed immunohistochemically with a polyclonal anti-estradiol-17β antibody, identified with a second antibody conjugated with peroxidase.

Results: The placental villi in all seven cryptorchid boys had a normal microscopic anatomical structure. The weak expression of the estradiol in the placentas of both the normal males and females was localized predominately as the basal part of the syncytiotrophoblast in the terminal placental villi. In contrast, all of the placentas of the cryptorchid boys had a strong expression of estradiol at the basal portion of the syncytiotrophoblast.

Conclusion: Our findings of an increased expression of estradiol as a result of an abnormal function of syncytiotrophoblast seemingly have an impact on testicular descent. This hypothesis may explain the nature of hypogonadotropic-hypogonadism found frequently in cryptorchid boys.

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PRETREATMENT TESTICULAR LOCATION: NO DIFFERENCE IN PATERNITY OF UNDESCENDED TESTIS AFTER UNILATERAL CRYPTORCHIDISM

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Background: Our previous studies have indicated that fertility (as indicated by paternity) is decreased after corrected unilateral cryptorchidism. Potential risk factors which impact infertility in unilateral cryptorchidism may include age of correction, preoperative testicular size, the development of the contralateral testis, and preoperative testicular location. It has been hypothesized that the higher the preoperative location the greater the risk of infertility. Thus, patients with abdominal testes may be at greatest risk for infertility.

Methods: The preoperative location of undescended testes has been compared with paternity among a cohort of formerly unilaterally cryptorchid men who had orchiopexy at the Children's Hospital of Pittsburgh. Data are presented only for men in the cohort who have fathered children or attempted conception with a partner for more than 12 months.

Results: Numbers and percentages of fertile and infertile men are listed for six preoperative locations, together with the percentage that had conception within 12 months.

<table>
<thead>
<tr>
<th>Location</th>
<th>Total</th>
<th>Successful</th>
<th>Unsuccessful</th>
<th>% with Conception &lt;12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal</td>
<td>32</td>
<td>26</td>
<td>6</td>
<td>64.5</td>
</tr>
<tr>
<td>Internal Ring</td>
<td>27</td>
<td>100.0</td>
<td>0</td>
<td>78.3</td>
</tr>
<tr>
<td>Canaliculal</td>
<td>117</td>
<td>103</td>
<td>14</td>
<td>70.5</td>
</tr>
<tr>
<td>External Ring</td>
<td>66</td>
<td>57</td>
<td>9</td>
<td>71.7</td>
</tr>
<tr>
<td>Ectopic</td>
<td>30</td>
<td>28</td>
<td>2</td>
<td>62.5</td>
</tr>
<tr>
<td>Upper Scrotum</td>
<td>8</td>
<td>7</td>
<td>1</td>
<td>85.7</td>
</tr>
</tbody>
</table>

Biopsies of the newborn placentas were fixed in glutaraldehyde and embedded in Epon for immunohistological procedures. The genitalia of the newborn were examined immediately after birth. Those boys with either unilateral or bilateral cryptorchidism were reexamined after one year and followed until treatment. Seven boys in this study had cryptorchidism: six unilateral, one bilateral. Semi-thin histological sections of placental biopsies of these seven boys together with seven randomly selected normal male and seven female placentas were analyzed immunohistochemically with a polyclonal anti-estradiol-17β antibody, identified with a second antibody conjugated with peroxidase.

Results: The placental villi in all seven cryptorchid boys had a normal microscopic anatomical structure. The weak expression of the estradiol in the placentas of both the normal males and females was localized predominately as the basal part of the syncytiotrophoblast in the terminal placental villi. In contrast, all of the placentas of the cryptorchid boys had a strong expression of estradiol at the basal portion of the syncytiotrophoblast.

Conclusion: Our findings of an increased expression of estradiol as a result of an abnormal function of syncytiotrophoblast seemingly have an impact on testicular descent. This hypothesis may explain the nature of hypogonadotropic-hypogonadism found frequently in cryptorchid boys.
Statistical analyses indicate no differences in paternity between any of the groups. Further, the portion in each group that achieved conception within 12 months did not differ.

**Conclusion:** These data indicate that fertility after unilateral cryptorchidism is not more compromised among those who had abdominal testes than those with testes at lower sites.

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DNA ORGANIZATION IN PATIENTS WITH A HISTORY OF CRYPTORCHIDISM

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**Background:** Somatic cell DNA is specifically organized into loop domains (60–100 kb) attached to a nuclear matrix. This specific DNA organization is necessary for normal cell function. We have previously shown that normal human sperm DNA is also specifically organized into loop domains (26 kb) attached to a nuclear matrix and demonstrated evidence for a DNA anchoring structure, 1 micron in diameter, to which long strands of DNA are attached following sperm decondensation. Because sperm DNA is so specifically organized, we believe that normal sperm DNA organization is necessary for normal sperm function, as seen in the somatic cell. Indeed, naked, unorganized DNA will not replicated when presented to the ovum void of its nuclear matrix. In this study, DNA organization was studied in sperm obtained from infertile men with a history of cryptorchidism.

**Methods:** Sperm from 7 infertile men with a history of cryptorchidism were assayed for DNA organization. Patient ages ranged from 24 to 42 years. All patients were infertile and had a history of unilateral cryptorchidism repaired surgically between the ages of 16 months to 9 years. To form DNA loops, sperm were treated with 50 mM Tris (pH 7.4), SDS, 2 M NaCl and 10 mM DTT. DNA loops were stained with EtBr. DNA was decondensed by dissipating the nuclear matrix using, 50 mM Tris (pH 7.4), NP-40, 2 M NaCl and 10 mM DTT. Decondensed DNA was stained with EtBr.

**Results:** In all 7 specimens tested, DNA loop domains did not form into orderly 26 kb loops as seen in fertile human sperm. Loop domains were irregularly shaped and differed greatly in size. The nuclear matrix was also abnormal. It was unstable, tended to dissipate, and was irregular in size and shape. When the nuclear matrix was dissipated with NP-40, DNA decondensation was incomplete and long DNA strands seen in normal sperm were not demonstrated. The presence of a DNA anchoring structure was, however, suggested as in fertile sperm.

**Conclusions:** This study demonstrates abnormalities in DNA organization in infertile sperm which may alter normal sperm function. We conclude that abnormal DNA organization within the sperm nucleus plays a role cryptorchidism associated infertility.

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INHIBIN B: AN INDICATOR OF SEMINIFEROUS TUBE IMPAIRMENT IN CHILDREN WITH CRYPTORCHIDISM

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**Purpose:** A common complication of cryptorchidism is seminiferous tubule dysfunction resulting in infertility. A direct hormonal bioassay of seminiferous tubule function would be useful in the diagnosis and management of children with conditions that involve the testis such as varicocele, interser states, traumatic injury, torsion of the spermatic cord, Prune Belly syndrome and cryptorchidism. Recent evidence now suggests that inhibin B may be the best available endocrine parameter of spermatogenesis in men. Inhibin B is produced by the Sertoli cell and is considered an important regulator of FSH secretion by a closed-loop negative feedback mechanism. This study examines the relationship between inhibin B levels and circulating gonadotropins in infants and children with cryptorchidism to establish whether inhibin B may be a possible indicator of seminiferous tubule damage.

**Material and Methods:** 64 children, age 3 months through 14 years, were enrolled in the study. 41 patients had unilateral cryptorchidism, 15 had bilateral cryptorchidism, and 8 had a vanishing or atrophic testis. Inhibin B, FSH, and LH were obtained in all patients prior to orchidopexy. Inhibin B levels was quantitated by a double-antibody enzyme-linked immunosorbent assay from Serotec Ltd. (Oxford, UK). Inhibin B control values were obtained from recently published data. Inhibin B levels were compared for the same age group of control boys using the Mann-Whitney rank sum test. Correlation between inhibin B, FSH and LH levels was determined with multiple regression using Spearman’s method.

**Results:** In the age group of 13–36 months, a statistically significant difference between median inhibin B levels in cryptorchid patients (87.2 pg/ml) and controls (180 pg/ml) was observed (p<0.001). No other age group showed a statistically significant difference, but all demonstrated median inhibin B levels below the 25th percentile. A negative correlation (r = -0.78) between FSH and inhibin B levels was found in the 10–14 year old cryptorchid patients (P = .008). No other correlation was found between FSH or LH and inhibin B levels for any age group. Position of the cryptorchid testis did not correlate with inhibin B levels. 49% of patients with unilateral cryptorchidism had inhibin B levels below the 25 th percentile, and of these patients, 50% had FSH levels above the median. Of children with bilateral cryptorchidism, 53% had inhibin B levels within the first quartile and of these, 50% had elevated FSH levels. 4/8 children with vanishing or atrophic testis had inhibin B levels below the 25th percentile. A negative correlation (r = -0.78) between FSH and inhibin B levels was found in the 10–14 year old cryptorchid patients (P = .008). No other correlation was found between FSH or LH and inhibin B levels for any age group. Position of the cryptorchid testis did not correlate with inhibin B levels. 49% of patients with unilateral cryptorchidism had inhibin B levels below the 25th percentile, and of these patients, 50% had FSH levels above the median. Of children with bilateral cryptorchidism, 53% had inhibin B levels within the first quartile and of these, 50% had elevated FSH levels. 4/8 children with vanishing or atrophic testis had inhibin B levels below the 25th percentile.

**Conclusion:** This study demonstrates a trend of lower inhibin B levels in children with cryptorchidism. This was statistically significant in children 13 to 36 months in age, and the trend continued into older age groups. Long term follow up will be required to determine whether inhibin B is diagnostic or predictive of seminiferous tubule dysfunction in children with cryptorchidism.

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IMPAIRED GONOCYTE TRANSFORMATION DUE TO ANDROGEN RECEPTOR DEFECT

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**Background:** A sharp increase in serum gonadotropins and testosterone and a simultaneous transformation of gonocytes (the fetal stem cell pool) into adult dark spermatogonia (the adult stem cell pool) occurs in normal male infants between 2–4 months of postnatal life. Previous studies suggest that the testicular histology of prepubertal boys with complete androgen insensitivity syndrome (AIS) is normal. This study examines the testicular development in prepubertal and early pubertal patients with complete AIS.

**Methods:** Fifteen patients with complete AIS were studied. The ages ranged from 1 month to 40 years. Twelve were prepubertal or early pubertal boys. All had intraabdominal or high inguinal undescended testes. All had bilateral testicular biopsies. The tissue was fixed in 1% glutaraldehyde, embedded in Epon for semithin light microscopy and electron microscopy.

**Results:** All 12 of the prepubertal/early pubertal patients had normal testicular development which was obvious even in the
one month old. Ten (80%) of the 12 had complete absence of adult
dark spermatogonia despite the fact that the total germ cell counts
were all within the lower limits of normal. This abnormality
indicates a failure of gonocytes to transform into adult dark sper-
matogonia. None developed primary spermatocytes between 3 and
6 years of age when transient meiosis normally appears. All
had severe Leydig cell hyalineplasia and normal Sertoli cell number
and structure. Ten (80%) of the older prepubertal/early pubertal
patients progressed to Sertoli cell-only syndrome. Two (20%) had
a few adult dark spermatogonia; these may represent the “incom-
plete variant” of complete AIS.

Conclusion: Both complete AIS and cryptorchidism are associated
with failure of transformation of gonocytes (the fetal germ cell pool)
into adult dark spermatogonia (the adult germ cell pool) which
normally occurs at 2–4 months postnatally and which is probably
testosterone dependent. In AIS, the “injury” is the androgen receptor
defect on Sertoli cells which blocks the paracrine effect of normal or
increased intratesticular testosterone levels and leads to hyperplasia
of Leydig cells. In cryptorchidism, the “injury” is hypogonadotropic
hypogonadism which causes hypoplasia of Leydig cells and reduced
levels of intratesticular testosterone. The histomorphometric pathol-
sy seen in semithin sections of testicular biopsies in these two
conditions are mutually supportive of the hypothesis that the trans-
formation of gonocytes to adult dark spermatogonia is testosterone,
not temperature, dependent. The fact that the complete and incom-
plete variants of complete AIS both have cryptorchid testes in intra-
abdominal and high inguinal positions adds further circumstantial
evidence in support of that hypothesis.

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HOW WELL DOES CONTRALATERAL TESTIS
HYPERTROPHY PREDICT THE ABSENCE OF THE
NONPALPABLE TESTIS?

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ter, Los Angeles, CA.

Background: In 1991, Koff reported that in boys 3 years of age or
younger with a unilateral nonpalpable testes (NPT), contralateral
tests hypertrophy (CH) to more than twice normal size (testes >
2cc in volume or >2cm in length) predicted monorchia. The
purpose of this report is to verify the “Koff” principle—the degree
to which CH predicts monorchia in boys with a NPT.

Methods: From May, 1993 to September, 1998, sixty patients
were evaluated for a unilateral NPT. Two patients who received
HCG and two patients who had signs of puberty were excluded.
The ages of the remaining 56 patients ranged from 7 months to 11
years (14 boys were >3years old). After confirming the nonpal-
able status of the side in question by using a lubricated exam, the
volume (using a Takihara orchimometer) and/or length of the con-
tralateral testis was measured. We correlated the finding of CH
(using Koff’s criteria above) with the presence or absence of the
NPT. We also recorded the degree to which contralateral testis
measurements of less than 2.1cm correlated with the presence or
absence of the NPT. 52 underwent laparoscopy and 4 had an open
exploration.

Results: 16 patients had CH (>2cm). 14 (87.5%) had monorchia
and 2 (12.5%) had an intraabdominal testis. 14 of 15 patients with
contralateral measurements of >1.7cm (9), 1.9cm (3), and 1.8cm (3)
had monorchia (93%) while 1 had a tiny ovotestis. Combining the
31 patients with contralateral measurements of >1.7cm, 28 (90.3%)
had monorchia. Of these 28 patients with monorchia, 15 had blind
ending vas and vessels proximal to the internal ring, 1 had no
visible vessels within 5 cm of the internal ring, and 12 had atrophic
cord structures in the inguinal canal. Of the 25 patients who had
contralateral measurements of <1.8cm, 13 (52%) had testes (11
intraabdominal, 2 canal).

Conclusions: CH is common in patients with NPTs. It was
present in 29% of the patients when it was defined as >2cm and
in 55% of the patients when contralateral measurements of
>1.7cm were included. CH (>2cm) predicted monorchia 87.5% of
the time. The predictive value changes slightly when lesser mea-
surements are included (>1.9cm = 92%, >1.8cm = 89.3%, and
>1.7cm = 90.3%).

CH allows us to inform parents preoperatively that their son
was most likely born with one testis, but exploration is still re-
quired. Laparoscopy is particularly advantageous because of the
high percentage of blind ending vas and vessels in these patients.

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COMPARATIVE ASSESSMENT OF PEDIATRIC
TESTICULAR VOLUME: ORCHIDOMETER VERSUS
ULTRASOUND

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Zurakowski, Stuart B. Bauer, Craig A. Peters, Anthony Atala,
P. L. Ephraim, and Alan B. Retik. Children’s Hospital, Boston.

Introduction and Objectives: The accurate measurement of testicular
volume has assumed increased importance in assessing the clinical
significance of varicocele in boys. A volume differential of 20 percent
has been regarded as an indication for surgery. Traditionally, testic-
ular volume in children has been measured with either the Prader or
Rochester (Takahara) orchidometers. Scrotal ultrasound has dem-
onstrated promise for achieving greater precision. The objectives of this
study are to answer 2 questions: 1) How closely do physician testicu-
lar volume measurements with Prader and Rochester orchidom-
eters correlate with ultrasound calculations? 2) How effective are
Prader and Rochester orchidometers compared to ultrasound in de-
tecting a percent volume difference between testes?

Methods: Sixty-five patients with a diagnosis of varicocele (58),
undescended tests (6), and testicular torsion (1), were studied, some
of whom had multiple measurements over time. Eighty testicles were
sized with the Rochester orchidometer and 75 with the Prader or-
chidometer and then compared to ultrasound evaluation. Forty stud-
ies of volumetric difference between testes were performed with the
Rochester and 37 with the Prader orchidometers and compared with
ultrasound measurements. The ability of each technique to distin-
guish a 10, 15, 20, and 25 percent volume difference between testes
was compared. Statistical analysis performed using Pearson’s corre-
lation coefficient, Kappa test and paired t-test.

Results:

Conclusions: 1) There is a significant correlation between
the Prader and ultrasound measurements and between the Rochester
and ultrasound sizes when measuring absolute testicular vol-
umes, but both orchidometers overestimate volume by 6cc com-
pared to ultrasound. 2) To distinguish a tesicular volume differ-
ential of 10, 15, 20, or 25 percent, neither orchidometer compares
favorably with ultrasound. Orchidometer readings have higher
specificity than sensitivity in determining tesicular volume dif-

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ferences. The specificity was better with the Prader than Rochester orchidometer.

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MICROSURGICAL LIGATION IN ADOLESCENT VARICOCELE. MUCH ADO ABOUT NOTHING?
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Background: Varicocele is a common cause of adult infertility and early repair has been advocated. High retroperitoneal ligation of spermatic vessels (Palomo approach) is one of the most popular operations because of the low recurrence rate. However, hydrocele formation can occur and the late effect of the artery ligation remains uncertain. For this reason microsurgical inguinal or subinguinal varicocelectomy has gained the favour of adult urologists. Recent report suggests that microsurgical repair during adolescence is effective and warranted (G.E. Lemack. J. Urol. 160: 179, 1998).

Methods: Sixty two patients affected by varicocele moderate to large, observed in 8 month period, were randomized to two groups. Group A: 32 left varicoceles operated on with Palomo approach (mean age 14.2 yrs, ± 2.8). Group B: 30 left varicoceles operated on with microsurgical (6 to 20 X magnification) subinguinal ligation of spermatic veins (mean age 14.9, ±3.2). Patients were then compared with regard to the parameters shown in the table. Statistical analysis was performed by student T test and Chi square test.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Palomo</th>
<th>Microsurgery</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>32</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Grade II</td>
<td>11</td>
<td>9</td>
<td>n.s.</td>
</tr>
<tr>
<td>Grade III</td>
<td>21</td>
<td>21</td>
<td>n.s.</td>
</tr>
<tr>
<td>Mean operative time</td>
<td>27 (13-40)</td>
<td>55 (42-68)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Immediate postoperative period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>testicular-epididymal pain</td>
<td>14</td>
<td>1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>abdominal pain</td>
<td>7</td>
<td>–</td>
<td>=0.002</td>
</tr>
<tr>
<td>transient hydrocele</td>
<td>2</td>
<td>1</td>
<td>n.s.</td>
</tr>
<tr>
<td>Normal activity after</td>
<td>7</td>
<td>5</td>
<td>n.s.</td>
</tr>
<tr>
<td>(days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up (mean 9, range 6-12 months).</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>recurrence</td>
<td>1</td>
<td>1</td>
<td>n.s.</td>
</tr>
<tr>
<td>hydrocele</td>
<td>3</td>
<td>2</td>
<td>n.s.</td>
</tr>
<tr>
<td>catch-up growth</td>
<td>24</td>
<td>26</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Conclusion: Frequent and rapid catch-up growth of the affected testis in both groups suggests that correction of varicocele during adolescence is probably the most effective policy to prevent male infertility. The technique used (whether traditional or microsurgical) appears to affect neither recurrence of varicocele nor complication rate. On these considerations there is evidence that microsurgical repair does not offer any significant advantage over conventional techniques.

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MALE SELF HEALTH AWARENESS
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Background: The purpose of this study is to examine male teenagers’ knowledge and understanding of the necessity for genital examination and the signs and symptoms of serious testicular pathology. Furthermore, current national guidelines for health education were reviewed in order to better understand the curriculum employed by the educational system and assess its effectiveness.

Methods: A five question survey was administered privately and confidentially to male athletes prior to sports physical in 1996 and 1999. Athletes were aged 12-18, attending middle or high school and sampled randomly. The Health Education National Standards Benchmark for grades 9 through 11 were examined with specific attention to male self health education standards.

Results: 318 athletes responded revealing that 46% did not know why the genitals were examined in the sports physical, 45% did not use appropriate testicular protection. On questions concerning acute testicular pathology, incorrect answers ranged from 36 to 85% of the respondents. Only 0.6% answered all questions correctly. Despite the fact that 54% of respondents answered that checking for a “hernia” is a reason for a genital exam, there was no mention of tumor, infection or varicocele. Review of HESN benchmarks revealed no standards referring to a minimum understanding of anatomy or physiology. Generalized guidelines for high risk behaviors were provided without specific mention of testicular torsion, cancer, varicocele or sexually transmitted diseases.

Conclusion: Young males are grossly unaware of many aspects of their self health. They are at higher risk for testicular torsion, cancer, and varicocele than any other age group, yet our population was universally unaware of any of these as a reason for genital examination. Furthermore, 99.4% did not respond appropriately to questions regarding serious testicular pathology. This is not surprising upon review of national guidelines. Provisions for male self health are poorly defined and very nonspecific. We have developed a curriculum for male self health to address this problem.

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HOW EFFICIENT IS THE PRENATAL DIAGNOSIS OF AMBIGUOUS GENITALIA?
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Background: The prenatal diagnosis of ambiguous genitalia may have a major impact on the prenatal counseling and the postnatal outcome. Our aim was to evaluate the incidence of genital anomalies diagnosed either by prenatal ultrasound or by neonatal examination in a tertiary center for fettal medicine, and to study the accuracy and clinical implications of a prenatal diagnosis of a genital malformation.

Methods: From 1992 to 1998, 2100 pregnant women were managed in the obstetric department of our institution. Among this cohort we reviewed 2 groups of cases: the first group were diagnosed prenatally as genital anomalies and their outcome was confirmed either postnatally or by fetopathologist if pregnancy termination was decided, the second group included children having genital anomalies which were not diagnosed prenatally. There were 61 cases included in this study. Isolated anterior hypospadias were excluded from this study.

Results: The genital anomalies were accurately described in 30 cases, were not detected prenatally in 21 cases, and in 10 cases the anomalies were absent at birth. Discordance between prenatal diagnosis and postnatal outcome was observed in 22 newborns. 12 newborns with genital anomalies were considered normal on the prenatal screening ultrasound. The anomaly was female pseudohermaphrodism (FPH) due to congenital adrenal hyperplasia (CAH) in 5; male pseudohermaphrodism (MPH) in 6; and female epispadias with clitorial duplication in one case. 10 newborns had prenatal diagnosis of genital anom-
aly and they were normal at birth. Prenatal diagnosis succeeded to make the exact description of the anomaly in 20 newborns. FPH was diagnosed in 6 cases, and their etiology was accurately suspected before birth: CAH in one and malformative FPH in 5 cases. MPH were diagnosed in 11 cases, they were suspected prenatally in front of a 46XY cariotype, penile chordee or micropenis and or uni or bilateral cryptorchidia. All these children have been raised as male after successful stimulation of penile growth by testosterone therapy. 3 cases of syndromic malformations including a genital anomaly had been accurately diagnosed prenatally. Termination of pregnancy was refused by the parents, and the 3 newborns had the described malformations and died shortly after birth. Termination of pregnancy was realised in 19 cases due to a polymalformative syndrome. Among these, the genital anomaly had been prenatally diagnosed in 10 cases and was discovered at the post-mortem exam in 9. There were 6 chromosomal anomalies; 6 syndromic malformations (2 VACTERL, 3 Smith-Lemli-Opitz, 1 Bonncire Ulrich syndrom) and 7 non-syndromic polymalformations.

Conclusion: Our results shows that the screening prenatal ultrasound was not sufficiently sensitive to detect genital anomalies. Meanwhile the prenatal diagnosis of genital anomalies was highly specific in cases of polymalformations.

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A COMPREHENSIVE ANALYSIS OF A TIP HYPOSPADIAS REPAIR

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Background: The tubularized incised plate (TIP) urethroplasty is a relatively new hypospadias repair that has gained widespread acceptance. The TIP hypospadias repair has been reported to provide excellent cosmetic and functional results with minimal complications. This study critically evaluates my experience using a TIP hypospadias repair.

Methods: Between September 1995 and January 1999, 64 boys ages 7 mos-11 yrs (mean 22.9 mos) underwent a TIP urethroplasty by a single pediatric urologist for primary hypospadias. The hypospadias defects included 53 distal (coronal or subcoronal) and 11 midshaft. The incision of the urethral plate was always deep and proximal but never extended the entire length of the plate. In 25 cases (39%) the incision was less than half the length of the urethral plate. A two-layer urethroplasty was always obtained. A vascularized subcutaneous pedicle was always placed onto the urethroplasty. This pedicle was ventrally-based in 56 (87.5%) of the repairs. Postoperative urethral stents were not used in 52 (81.3%) boys including 7 with midshaft repairs. None of the cases required corporal plication. All children were scheduled for a postoperative evaluation at 1 month. A confidential phone survey was later conducted by someone other than the surgeon. The parents were asked if they were satisfied or unsatisfied with (1) direction and caliber of the urinary stream, (2) chordee correction and (3) overall general appearance.

Results: There were no intraoperative complications. Clinical evaluation was performed in 54 (84.7%) boys not earlier than 1 month after repair. Exam revealed a conical glans, slit meatus, circumferential mucosal collar, and a straight phallus in all cases. There were no cases of fistula, stricture (namely meatal stenosis) or dehiscence. Follow-up phone survey 3–43 mos (mean 21.0 mos) postoperatively was obtained from the parents of 40 patients. Without exception, all parents were satisfied with the urinary stream, chordee correction, and overall appearance.

Conclusion: Without incising the entire urethral plate and stenting the repair, a TIP urethroplasty can still be expected to provide excellent results when correcting distal and midshaft hypospadias. Parents are satisfied with the long term cosmetic and functional results that are obtained with a TIP urethroplasty.

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SNODGRASS HYPOSPADIAS REPAIR WITHOUT CIRCUMCISION

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Background and purpose: The aim of distal hypospadias repair is to obtain a straight and functional penis with normal cosmetic appearance. In our population, this concept is frequently related to prepuce preservation, so that, postioplasty is nearly always preferred to circumcision, even in phimosis surgery. We describe here our results with distal hypospadias repair and simultaneous preputial reconstruction.

Methods: In the last two years we have replaced classical Mathieu repair for distal hypospadias with the Snodgrass procedure. The preputial reconstruction is easier to perform with this technique, since there are more skin available, because it is not necessary for urethral reconstruction. We have performed Snodgrass operations in this period combined with preputial reconstruction in 41 patients between 5 months and 14 years old. After performing urethroplasty, meatus repair and glanuloplasty two traction sutures pick up both corners of the open prepuce, this step allows approximation of both ends to ventral midline to test the cosmetic result and to obtain a retractable prepuce. Two vertical incisions are performed joining the traction sutures and the free ventral border of the prepuce to create the inner and outer faces of the postioplasty, that later on are brought together with interrupted sutures.

Results: Complications were one complete dehiscence, two partial dehiscences with urethral fistula and a solitary fistula in another patient. All these patients needed only one reoperation 6–8 months after the original procedure. The complete dehiscence needed an island flap onlay procedure and circumcision. The aesthetic postoperative appearance was satisfactory in nearly all patients, as the penis looks normal and uncircumcised as it was the parent’s desire.

Conclusion: It is feasible to obtain a normal uncircumcised penis in anterior hypospadias reconstruction with Snodgrass technique. A slightly higher rate of complications are expected but the final aesthetic aspect of the penis outweighs these inconveniences.

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HISTOLOGY OF THE URETHRAL PLATE: IMPLICATIONS FOR HYPOSPADIAS REPAIR

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Background: Recently, hypospadias repair based entirely upon the urethral plate has gained widespread popularity. Nevertheless, uncertainty exists regarding the nature of these tissues; some describe the plate as "healthy" and "pliable" while others believe it consists of epithelium overlying fibrotic tissues. In the latter description these presumably dysplastic remnants of urethral formation are said to tether the corpora cavernosum, resulting in ventral penile curvature. We report histologic examination of the urethral plate to help resolve this controversy.

Methods: Subepithelial biopsies of the urethral plate were obtained in 10 boys during primary hypospadias repair, including 7 with distal shaft and 3 with penoscrotal anomalies. Artificial erec-
tion demonstrated ventral curvature in 3 patients, all with penoscrotal hypospadias. In one boy with penoscrotal hypospadias the urethral plate visibly tethered the penis, and so required transection to achieve straightening. In this case the full thickness of the plate was available for histologic evaluation, while in the remainder biopsies were taken from the depths of the plate after its midline incision.

Results: All biopsies demonstrated the subepithelial component to be well vascularized connective tissue, comprised of collagen and smooth muscle interspersed with blood vessels and nerves. In no case was fibrous scar tissue found. Also, there was no histologic distinction between urethral plate biopsies in patients with versus without penile curvature.

Conclusions: The urethral plate consists of epithelium overlying well-vascularized connective tissue. We found no histologic evidence to support the hypothesis that fibrous tissues of the plate contribute to penile curvature. From a histologic standpoint, preservation of the urethral plate and its incorporation into hypospadias urethroplasty appear to be sound clinical options unless a foreshortened plate tethers the penis.

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THE GITUP (GLANULOPLASTY AND IN SITU TUBULARIZATION OF THE URETHRAL PLATE) HYPOSPADIAS REPAIR: A SIMPLE TECHNIQUE FOR DISTAL HYPOSPADIAS REPAIRS.
Andrew K Chung, MD and Evan J Kass, MD FAAP. Dept of Urology, William Beaumont Hospital, Royal Oak, MI.

Background: In 1995 we initially described the GITUP hypospadias repair which involves tubularization of the urethral plate in order to produce a normal appearing urethral meatus. This technique incorporates elements of the King and Thielsch-Duplay techniques for hypospadias repair. Subsequently, Snodgrass described a similar procedure that required incision of the urethral plate in order to create a neourethra of greater caliber. We have not found this modification necessary in the vast majority of children and herein describe the GITUP hypospadias repair in 308 children without incision of the urethral plate.

Methods: The original paper describing the GITUP technique in 1995 reviewed 166 patients. We have since reviewed an additional 142 patients for a total of 308 patients. Follow-up consisted of patient visits at 1 week, 6 week and 1 year intervals. Telephone contact was attempted if one year follow-up was not obtained. If there were no complications at one year, the patient was discharged from follow-up unless further problems occurred.

Results: Overall cosmetic results were excellent. Our overall complication rate was 9.4%, and consisted of a urethral fistula (8.4%) and two urethral diverticula (0.6%). There was no evidence of meatal stenosis, urethral stricture, residual chordee, balanitis or hematoma formation. In addition, in comparing the last 142 patients with the first 166, we have noted that our complication rates have dropped from 8% to 1.7% in patients with a distal/coronal hypospadias, and from 20% to 7.7% in patients with a midshaft hypospadias. We believe that this is due to the addition of a third layer of spongy tissue and a subcutaneous transverse island flap in the repair for most patients. Also of note, only 4 of the 29 complications occurred after the first year (13.8%). Thus, it appears that the functional durability of the repair has been lasting.

Conclusion: The GITUP hypospadias repair is a simple, reliable and durable technique for distal hypospadias repairs with a low complication rate.

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OUTCOME ANALYSIS OF TUBULARIZED INCISED PLATE HYPOSPADIAS REPAIR
Antoine E. Khoury MD FAAP, Alpana Prasad MD, Paul A. Mergeruan MD FAAP, Gordon A. McLorie MD FAAP, Darius J. Bagli MDCM FAAP. The Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada.

Purpose: We reviewed our experience using the tubularized incised plate (TIP) urethroplasty to correct distal hypospadias and compared surgical outcomes of stented and unstented repairs. We also evaluated the impact of using vascular pedicle to cover the reconstructed urethra.

Methods: A total of 124 boys underwent TIP repair between September 1996 and October 1998. 117 were primary repairs, while 7 children underwent TIP repair as a secondary procedure.

Results: Good cosmetic and functional results with a vertically oriented meatus at the tip of the glans, was achieved in 88% of cases. Complications, including small urethrococutaneous fistulas (8), meatal stenosis (4), stricture (1), meatal recession (1) and urethral diverticulum (1), occurred in 15 children. The majority of the complications occurred early in our experience. In the last 50 patients, there were only two complications (4.0%).

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No. patients</th>
<th>No. Fistulas (%)</th>
<th>No. other complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary repair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stented</td>
<td>89</td>
<td>7 (7.8%)</td>
<td>5 (5.6%) (meatal stenosis 3, stricture 1, meatal recession 1)</td>
</tr>
<tr>
<td>Unstented</td>
<td>28</td>
<td>1 (3.5%)</td>
<td>1 (3.5%) (urethral diverticulum)</td>
</tr>
<tr>
<td>Vascular cover present</td>
<td>93</td>
<td>7 (7.5%)</td>
<td>5 (5.3%) (meatal stenosis 3, diverticulum 1, meatal recession 1)</td>
</tr>
<tr>
<td>Vascular cover absent</td>
<td>24</td>
<td>1 (4.1%)</td>
<td>1 (4.1%) (stricture)</td>
</tr>
<tr>
<td>Secondary repair</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stented</td>
<td>5</td>
<td>0</td>
<td>1 (meatal stenosis)</td>
</tr>
<tr>
<td>Unstented</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusion: TIP repair of hypospadias produces excellent cosmetic results with minimal morbidity. The presence or absence of stent and an additional cover of vascularized tissue did not adversely affect the outcome in our small series.

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MANAGEMENT OF PENOSCROTAL TRANPOSITION: A NOVEL APPROACH
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Background: The standard means of managing the patient with penoscutal transposition has always relied on the creation of scrotal, penile and suprapubic skin flaps. In many cases this portion of the procedure would have to be postponed if it was done in conjunction with a hypospadias repair or chordee correction because of fears of compromising the skin flaps used to cover the penile shaft. A novel approach was devised by one of the authors (EFR) that facilitates its correction and is cosmetically superior to present techniques.

Methods: Six boys ages 10 months to 9 years were operated on for severe penoscutal hypospadias and chordee. All patients required dermal grafts to correct their extraordinary chordee. The penis was degloved in the standard fashion maintaining a thick dorsal pedicle of dartos on the penile shaft skin. The penile shaft skin was split down the midline along the ventrum and then detached at the penoscutal junction by making a circumferential incision while preserving the lateral subcutaneous blood supply. A buttonhole incision was made where the penis should be in the suprapubic skin and the pedicle of penile skin is transferred along with the penis through the buttonhole. The penile skin is then reapproximated to the shaft after the chordee is corrected. A scrotoplasty is then performed if a bifid scrotum is present.

Results: All 6 patients had excellent cosmetic results with no loss of any of the transposed flaps. The results were superior to those achieved by conventional means.

Conclusion: This novel approach to a difficult problem has provided cosmetic results that are superior to standard means. In the extraordinary case this has become the preferred means of managing this problem.

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CLOACAL EXSTROPHY: MANAGEMENT OF THE 46XY GENOTYPE

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Introduction: Cloacal exstrophy is the most severe of the ventral abdominal wall deformations. Survival is now possible in the majority of these infants. Therefore, quality of life issues and sexual reassignment are now the focus of attention. We report the evolution in the management of a large group of patients born with cloacal exstrophy and a 46XY genotype.

Methods: We reviewed the medical records of patients diagnosed with cloacal exstrophy or cloacal exstrophy variant treated over the past 20 years. The records were examined to determine the genotype, sex of rearing, surgical therapy, and current quality of life.

Results: A total of 55 patients diagnosed with cloacal exstrophy during a 20 year period was identified. Thirty patients had a 46XY genotype. Of these XY patients, 16 were raised as males and 14 were gender reassigned at birth. Newer surgical techniques, such as complete penile disassembly and complete primary repair of exstrophy, are instrumental in maintaining genetic sex assignment. Therefore, during the past 10 years, only 1 patient with a 46XY genotype underwent sexual reassignment. Fourteen of the 16 patients raised as males are alive and functioning well in society. Two of the males died in their twenties as a result of sepsis and renal failure, respectively. Currently, the patients raised as males range in age from 1 year to 24 years (mean 9.7 years). At birth, 3 were described to have a bifid phallus while 10 had a small epispadiac phallus. Three males were exstrophy variants with an intact phallus and hypospadiac urethra. Prior to 1989, the urethral plate was divided and paraeystrophy flaps were utilized in reconstructing the epispadiac urethra. More recently, however, 4 males underwent complete primary repair of exstrophy without division of the urethral plate. At the time of initial bladder closure the urethra could only be brought to the penoscutal junction in these patients. Subsequently, a second stage Thiersch-Duplay type of urethroplasty was performed. To date, none of the 4 patients required augmentation or rely on catheterization to empty their bladder. The upper tracts and renal function remain stable in these patients.

Conclusion: The patient born with cloacal exstrophy and a XY genotype presents a formidable challenge. In the past, most of these children were raised as females. Since there is no long term psychological data on this group of children, each patient must be treated on an individual basis. However, with newer surgical techniques the majority of patients can be raised in accordance with their genetic sex. Further close follow-up on this group of children will be important in determining their psychosocial outcome.

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ADULT CLINICAL, PSYCHOSOCIAL ADAPTATION IN PATIENTS BORN WITH BLADDER EXSTROPHY

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Goal: To assess the clinical, psychosexual and social adaptation after a mean of 25 years of follow-up, in bladder exstrophy patients treated with internal rectal bladders.

Material and Method: 26 out of 31 patients accepted to participate in the study, in which Renal function, hypercloremic acidosis, DMSA scan, neobladder volume, fecal and urine continence and rectal biopsy was done in the clinical trial. And SCL90; Personality EPQ, A, and Despair scale BECK.ED tests plus a personal interview with our phycologists to asses psychosexual and social adaptation as adults.

Results: Clinical 24 had normal creatinine and GFR values, 2 had 1.5 mgs./dl, and mild degree of concentration deficit. Both had moderate Hypercloremic acidosis. DMSA scan was normal in 20, 2 had focal unilateral scars, and four had bilateral focal and diffuse lesions, only two lost 20 % of unilateral function. Fecal continence was present in 100 % and Urinary continence in 96 %. Six patients got continence after neobladder ileal augmentation with an mean increase in volume of 290 ml (range 190–370 ml). All patients had one or two genital reconstructions. Mean genital and urinary reparation rate 1.61 %/ pat.

Psychological: SCL 90 show 1 women is over mean values, two men and a woman in mean values and 22 under mean values. Which represents an interpersonal relationship similar to normal population. EPQ. A personality test shows 11 emotional instability, 9 within normal range and 6 under. High degree of sincerity. BECK.ED despair test showed 23 with a positive attitude in life three were negative but none showed suicide index. Personal interview reveal in all suffering as children that increased in puberty, anxiety and fear to find a partner. Sexual relations, 2 women and 3 men had never a couple. Three of them had sexual satisfaction through masturbation. Ten had relation with couple. Nine had normal complete stable and satisfactory relationship six have fathered a child. One divorced. Socially dependant on strong family relationship, many feel alone and ask for help. Six abandoned studies and do not qualified labour work, 12 finish school and are doing qualified work, and six finished or are in university studies.

Conclusions: Duhamel-Monereo rectocistoplasty not in use nowadays, is a technique that preserves renal function and gives fecal and urinary continence in the long term. Social and psychologic relationship is not very different to normal population apart from more suffering and depression, and sexual shyness. We could have helped them with more information from birth, and psychological assistance through puberty.
THE USE OF PELVIC OSTEOTOMY IN REPAIR OF BLADDER EXSTROPHY

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Background: To assess results, applications, and complications of pelvic osteotomy producing continence in patients with the exstrophy/epispadias complex.

Methods: Eighty-five patients who underwent pelvic osteotomy and external fixation were reviewed at a minimum of two year follow up (mean 4.8 years). Seventy-two patients had classic bladder exstrophy and 13 patients had cloacal exstrophy. Indications for osteotomy were to achieve a tension-free closure of the bladder and lower abdominal wall and/or to approximate pelvic floor muscles at the time of later bladder neck reconstruction. The patients were stratified into five different groups of age at surgery for analysis. Of these patients, 37 had anterior innominate osteotomy, 40 combined anterior innominate and posterior iliac osteotomy, 6 posterior iliac osteotomy, and 2 suprapubic ramotomy osteotomies were performed.

Results: The mean age at surgery was 2.9 ± 3.7 years (range 3 days to 13 years old). Osteotomy was performed at the time of initial bladder closure in 21, reclosure in 34, and bladder neck reconstruction in 30. In classic exstrophy patients, diastasis was corrected to an initial mean of 2.8 cm and a final mean of 3.8 cm. Cloacal exstrophy patients had significantly greater initial and residual diastasis. Maintenance of diastasis correction increased continuously with age at surgery. Wound dehiscence or bladder prolapse occurred in 4% of patients after primary closures and 0% after reclosure. Daytime continence was achieved in 75% of patients. The degree of continence was not correlated with percent correction of diastasis. Complications include transient femoral nerve palsy in 7 cases (8%) which all resolved spontaneously after three months and were probably due to tension on the inguinal ligament; delayed union in 3; late pin-track osteomyelitis in one.

Conclusion: Pelvic osteotomy is useful in helping achieve two goals of exstrophy treatment: successful bladder and abdominal wall closure along with urinary continence. The authors prefer an anterior approach because of the single stage positioning and accuracy of fixator application. Long-term maintenance of diastasis is least in the younger patients, probably because of continued undergrowth of the anterior pelvic segment. The authors prefer closure without osteotomy in young infants if this can be achieved early on without tension. However, in other cases, pelvic osteotomies are effective in achieving treatment aims with an acceptably low complication rate.

RESULTS OF UMBILICOPLASTY FOR BLADDER EXSTROPHY

Christian Pavlovich, MD, Jeffrey Stock, MD, FAAP and Moneer Hanna, MD, FAAP. New York Hospital-Cornell Medical Center, New York, N.Y. and Children’s Hospital of NJ, St. Barnabas Health System, Livingston, NJ.

Background: The umbilicus is an important aesthetic landmark and it’s absence or deformity may be associated with poor self-image. In patients born with bladder exstrophy the umbilicus is attached to the upper margin of the bladder and reconstructive surgery often removes the navel. Restoration of the umbilicus marks the waistline and serves to complete the harmony of the curved lines above and below. Umbilical reconstruction is generally appreciated most by older children and their parents.

Method: Our database included 61 children born with classic bladder exstrophy and 8 children born with cloacal exstrophy. These children were treated between 1980 and 1998. In 35 children (Group A), the primary reconstruction was performed by us. 34 children and young adults (Group B) were referred for secondary surgical repair, which included bladder augmentation, continent diversion, genitoplasty … etc. Neumobiloplasty was performed in all children in Group A, and in 30/34 in Group B. Early in the series a V-shaped flap was raised and buried subcutaneously. The flap eventually became a tube around the cystotomy tube and the cicatrix formed the umbilical dimple. This method necessitated packing with iodoform gauze for four weeks and weekly dressings. The technique evolved to a tubulized U shaped flap. A rubber tube is placed inside as a stent to maintain the inward projection of the neumobilus. This latter method allowed for healing by primary intention, and is preferred to the former method, where healing is by secondary intention.

Results: The early results of 69 umbilicoplasties were described by the surgeon as excellent or satisfactory in 66/69. In three cases the neumobilicus appeared flat, lost its depth and was described as unsatisfactory. Long term follow up (more than 1 year) was available in 48 patients. 2/48 underwent umbilical repositioning as the umbilicus was off center or too low. 3/48 underwent redo umbilicoplasty due to flat umbilicus, which had lost depth. The best cosmetic results were achieved in patients with a relatively thick layer of subcutaneous fat (chubby children), whereas thin children had suboptimal cosmetic results. Nonetheless the patients and their parents were generally pleased with the umbilical appearance, even when the surgeon was not.

Conclusion: Although the navel is a functionless, depressed scar, it represents an important and pleasing landmark. The waistline demarcates the distinction between the upper and lower body, and the navel serves as a reference point. Umbilical construction should be attempted early, either during functional closure or urinary diversion. At present we bring the cystotomy and ureteral stents through the tubulized flap, as this has proven to be both simple and reliable.

THE ROLE OF IDIOPATHIC HYPERCALCIURIA IN A SUB GROUP OF DYSFUNCTIONAL VOIDING SYNDROMES OF CHILDHOOD

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Background: Idiopathic hypercalciuria is believed to be the cause of a variety of urinary tract complaints in clinical pediatrics. These complaints include urinary frequency, urgency, dysuria or a combination of the above, often associated with gross or microscopic hematuria. In children, non-calculus manifestations of idiopathic hypercalciuria are reportedly more common than urolithiasis. Our aim was to determine the utility of Ca:Cr ratio in the evaluation of different subsets of functional voiding disorders.

Methods: Two hundred and eighty eight patients (288) with functional voiding disorders were evaluated over the last 8 years. Patients presenting with isolated urinary tract infection were not included. A thorough history with emphasis on voiding patterns was elicited and a routine urinalysis was performed in all patients. Based on the above, the patients were divided into 5 groups: Twenty two (22) patients had gross hematuria with dysfunctional voiding pattern (GH+DVP), 102 patients had microhematuria with DVP (MH+DVP), 66 patients had isolated Daytime Frequency of Childhood (DFOC), 45 patients had isolated Dysuria syndrome and 53 patients had combined frequency-urgency-dysuria syndrome (F+U+D) of childhood. The season of presentation was noted to determine a seasonal pattern, if any. A total of 149 patients from the above groups had their urine evaluated for a spot Calcium: Creatinine (Ca:Cr) ratio.
The patients were treated predominantly with behavioral therapy and correction of faulty voiding habits, antibiotics and anticholinergics and some patients were put on minor diet modification. A mean follow-up of 6.5 months (range 1 month-10 years) was available in a total of 153 patients (53%) from the above groups. Resolution of symptoms along with marked improvement in voiding habits was seen in 136 patients (89%), a moderate improvement in symptoms was seen in 10 patients (6.5%), and 7 patients (4.5%) had persistent symptoms with minimal improvement. Treatment with thiazides was used in only 6 patients (2%) who had intractable symptoms and a markedly elevated urine Ca:Cr ratio, of whom 5 patients responded favorably.

Conclusion: Idiopathic hypercalciuria may play a significant role in patients with functional voiding disorders. It affects the different subsets of voiding disorders with remarkable consistency, though its exact mechanism remains unknown. Although a significant number of patients with voiding dysfunction do have an elevated Ca:Cr ratio, the majority of these patients respond nicely to the standard behavioral therapy and pharmacotherapy in the form of antibiotics and anticholinergics and treatment directed to hypercalciuria is not required in most cases.

2

THE DYSFUNCTIONAL VOIDING SCORING SYSTEM (DVSS): OBJECTIVE CRITERIA FOR EVALUATION OF VOIDING DYSFUNCTION IN CHILDREN

Walid Farhat MD, Darius J. Bägli, MDCM FAAP, GianPaolo Capolicchio MDCM, Sheila O'Reilly, RN, Paul A. Merguerian MD FAAP, Antoine Khoury MD FAAP, Gordon A. McIlorie MD FAAP. The Hospital for Sick Children, University of Toronto, Toronto, Canada.

Purpose: The impact of acquired voiding dysfunction (DV) on the social and urologic health of the individual child is well recognized. However, due, principally to the lack of available measurement instruments to describe DV, the literature is devoid of studies which provide objective, meaningful assessment of diagnosis or treatment response, either within or across various DV populations. This study evaluates the performance of a newly devised objective instrument to quantify pediatric DV symptoms in a children’s hospital. The Dysfunctional Voiding Scoring System (DVSS) is a child-specific modification of the American Urological Association Scoring System for BPH (IPSS).

Materials and Methods: Ten voiding dysfunction parameters were assigned scores of 0 to 3 according to prevalence: 'not-at-all' = 0, 'less than half the time' = 1, 'half the time' = 2, 'almost always' = 3. One of the 10 parameters included assessment of specific child-life stresses ('absent' = 0, 'present' = 3). The total score ranged from 0 to 30. Unlike the BPH/IPSS scoring system, the urology nurse administered the DVSS with responses obtained from parent and/or child. Consecutive patients (age< 3 to 10 years) presenting to the Pediatric Urology Clinic, with a history of diurnal urinary incontinence, urinary tract infections, or vesico-ureteral reflux, were evaluated with the DVSS. A second aged matched group consisted of children without suspected voiding dysfunction from the non-diabetic endocrine clinic.

Results: Ninety-five (33%) were male, 193 (67%) were female. The mean age was 6.1 (range 2–14 years), and the mean length of symptoms was 10 months (range 1 week-10 years).

<table>
<thead>
<tr>
<th>GH + DVP</th>
<th>MH + DVP</th>
<th>Pure DFQOC</th>
<th>Pure Dysuria</th>
<th>F+U+D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total pts.</td>
<td>22</td>
<td>102</td>
<td>66</td>
<td>65</td>
</tr>
<tr>
<td>Urine Ca:Cr</td>
<td>14</td>
<td>63</td>
<td>38</td>
<td>27</td>
</tr>
<tr>
<td>Hypercalciuria (%)</td>
<td>4 (28)</td>
<td>19 (30)</td>
<td>8 (21)</td>
<td>6 (22)</td>
</tr>
</tbody>
</table>

Results: 35 patients with clinically suspected voiding dysfunction were evaluated with the DVSS. Female: male ratio was 16:1. Scores were elevated (>10) in 32 of 35 children. Mean symptom score in the group with suspected voiding dysfunction was 15.4/30. In the subjects without suspected voiding dysfunction (n=14), female to male ratio was 2:1, scores were ≤10 in 13 of 14, and mean symptom score was 3.5/30. Using a score of >10 to define potentially significant voiding dysfunction, the DVSS shows a sensitivity of 97%, specificity of 76%, positive predictive value 88%, and negative predictive value 93% (Chi-square). The individual scores in both groups are depicted. The means were significantly different (p<0.00001, Student’s t-test).

Conclusion: The DVSS instrument appears to provide an accurate and objective (i.e., numerical) description of voiding behaviors in children. Furthermore, it appears able to accurately predict the presence or absence of DV in individual children (i.e., score performance by sensitivity, specificity, positive and negative predictive values) as well as significantly discriminate between the presence or absence of DV across different groups (p<0.00001). The threshold score (>10) appears to capture clinically relevant voiding dysfunction behaviors. However, in future assessments of the DVSS, the threshold score may need to be ‘tuned’ up or down as we learn to quantify the true impact of DV on co-existent abnormalities such as reflux or posterior urethral valves. Once validated by other centers, such an instrument will become an invaluable clinical, research, and outcomes analysis tool in the study of this protean clinical entity.

3

STRUCTURAL CHANGES IN THE BLADDER WALLS OF PREGNANT AND HORMONE TREATED RATS: CORRELATION TO BLADDER DYNAMICS

Larissa V. Rodríguez, Bingyin Wang, Steven P. Lapointe, Linda M. Dairiki Shortliffe. Stanford, California. (Presented by Dr. Rodríguez)

Purpose: Pregnancy is a period of profound hormonal and physiologic changes. We evaluated the effects of estrogen, progesterone, and pregnancy on bladder dynamics and studied the associated histologic and structural changes seen in the bladder wall.

Methods: Adult female Sprague-Dawley rats were studied and treated with different hormones: Group A-6 nonpregnant normal controls (NC), Group B-7 pregnant rats (PG), Group C-6 oophrectomized estrogen treated rats (ES), Group D-6 oophrectomized progesterone treated rats (PR), Group E-4 oophrectomized controls treated with seed oil (OO). Bladder pressures were recorded during filling and emptying at varying urinary flow rates. The bladders were harvested and placed in 10% formalin prior to being embedded in paraffin and sectioned. Masson’s trichome staining was performed on all specimens. Quantitative morphometric analysis was performed with a computerized image analyzer. Ratios of connective tissue to smooth muscle areas were determined in duplicate, Immunohistochemistry studies were performed to evaluate the distribution and expression of Collagens I, III, and IV and parathyroid hormone-related protein (PTHrP)
using monoclonal antibodies. The samples were stained in duplicate, each serving as its own negative control. Specific PTHrP expression was confirmed by using PTHrP derived peptides from a different region of the molecule to which the monoclonal antibody was raised.

Results: PG rats had significant increase in bladder capacity. PG and PR rats had increased bladder compliance at varying bladder capacity during different urinary flow rates as compared to NC and OO rats (p<0.05). This corresponded to morphometric analysis with bladders of PG and PR animals having lower connective tissue:smooth muscle ratios as compared to NC, ES and OO animals (p<0.05). Collagen I was increased in lamina propria of PG, OO and ES rats and the detrusor muscle layer showed differences in PG and PR groups as compared to all other animals with increased localization of Collagen III in the interfascicular space. No changes in the distribution of Collagen IV was noted. PTHrP was mainly in muscle cells in NC, ES and OO rats while in PG it was in connective tissue; PR animals showed increases in both connective tissue and muscle.

Conclusions: PR and PG rats have increased bladder compliance as compared with NC, OO, ES rats. These changes parallel structural changes seen in the bladders specifically in the ratios of connective tissue to smooth muscle, and the distribution and expression of Collagens I and III and PTHrP and may have age-related implications in the urinary tract.

4
IS PROACTIVE CLEAN INTERMITTENT CATHETERIZATION SAFE AND PRACTICAL IN NEWBORNS WITH SPINAL DYSRAPHISM?
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Background: Clean intermittent catheterization (CIC) is undertaken in children with spinal dysraphism to prevent deterioration of the upper urinary tract due to poor emptying or hostile bladder dynamics. CIC may play an important role in the management of the newborn with spinal dysraphism. There are few reports assessing the safety of CIC in newborns. This retrospective study was devised to assess the safety and practicality of our protocol based on proactive CIC in newborns with spinal dysraphism.

Methods: We reviewed the medical records of 106 children who presented at our institution with the diagnosis of spinal dysraphism from October 1990 to July 1998. Of these, 81 presented in the first 2 days of life and comprise our study population. Our protocol directs that newborns with spinal dysraphism begin CIC with an 8 Fr catheter every 4 hours. We decrease the frequency of CIC when the random urine volume is consistently < 20cc. A video-urodynamic study (UDS) is performed between 6 to 12 weeks of age.

Results: Forty-nine of the 81 infants were female and 32 were male (ratio 1.5:1). All but one patient was started on our CIC protocol at the time of diagnosis. One boy was not included on the CIC protocol due to difficulty in catheterization secondary to a small urethra. Of the 80 patients that started on CIC, 28 (35%) remained on CIC at the time of discharge. Of these 28 children, 17 (61%) continued CIC following the first UDS. Of the 52 children who were not on CIC at discharge, 3 (6%) were restarted after the first UDS because of poor emptying or increased bladder hostility. The only complication encountered with CIC was an increased incidence of urinary tract infections (UTIs), which occurred in 18 (58%) of the 31 children who were on CIC, versus 18 (37%) of the 49 who were not continued on CIC. The majority of infections were consistent with cystitis. Vesicoureteral reflux was seen during the first UDS in 7 of 28 (25%) children on CIC and in 11 of 52 (21%) not on CIC at time of hospital discharge. There were no cases of urethral stricture or false passage with a mean follow-up of 3 years. Following the initial teaching, all families readily accepted CIC.

Conclusions: The use of CIC in newborns is safe. The only complication was an increased incidence of UTIs. Our protocol proactively identified 17 (85%) of the 20 patients that required CIC based on our initial videourodynamic assessment. In addition, families were well prepared to begin CIC when it was started after the newborn period. Proactive CIC in the newborn with spinal dysraphism is safe and practical.

5
OUTCOME OF GASTROCYSTOPLASTY IN TERTIARY PEDIATRIC UROLOGY PRACTICE.
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Background: The use of stomach in bladder reconstruction has become popular over the last decade. However, its use is not a panacea and unique complications may occur. We herein review our experience with augmentation gastrocystoplasty.

Methods: A retrospective chart review of all gastrocystoplasties performed at Hôpital Sainte-Justine (Montreal, Quebec) and Children’s Hospital (Winnipeg, Manitoba) between December 1990 and December 1998 was undertaken.

Results: Twenty-three patients (11 F / 12 M) aged 1.5–22.5 years (average 10) underwent gastrocystoplasty in this interval. Primary diagnoses: spinal dysraphism (14), posterior urethral valves (3), cloacal exstrophy (2), cloacal outlet anomaly (2), multiple failed ureteric reimplantations with bladder dysfunction (1), and neurogenic bladder of uncertain etiology (1). Three patients were in chronic renal failure at the time of presentation. Reconstructive surgery concurrent with gastrocystoplasty included: ureteric reimplantation (10), bladder neck plasty or closure (8), and continent urinary diversion (5). Acute postoperative complications comprised urosepsis (2), bowel obstruction (2), and ureteric obstruction (1). Long-term complications encompassed hematuria/dysuria syndrome (4), inability to catheterize (3), perineal urinary fistula (2), continent stomal stenosis (1), new onset right hydronephrosis (1), and bladder calculus (1). Follow-up from the time of gastrocystoplasty ranged from 4–86 months. Of the twenty-three patients in this study, 16 were on proton pump inhibitors and/or H2 antagonists to prevent hematuria. In three patients, the hematuria/dysuria syndrome was poorly controlled medically, and they required conversion to another form of urinary reconstruction. Of twenty patients for whom VCUG results are available, the majority (18/20) is free of vesicoureteric reflux. For the 21 patients for whom post-operative ultrasounds are available, in all but three the upper tracts remained stable or improved. Intermittent catheterization is necessary in 19/22 patients and of those catheterizing, 12 are completely dry.

Conclusions: The use of stomach for bladder augmentation may be considered in patients with complex anomalies such as cloacal exstrophy and/or in patients with renal dysfunction and metabolic acidosis. However, most patients will require histamine blockers and/or proton pump inhibitors to prevent the occurrence of gross hematuria. The symptoms of hematuria/dysuria can be disabling, especially in sensate patients, and may require alternative forms of urinary reconstruction such as a composite bladder augmentation incorporating ileum.
IN VITRO ENGINEERING OF HUMAN STRATIFIED UROTHELIUM: ANALYSIS OF ITS MORPHOLOGY AND FUNCTIONALITY

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Background: Bladder augmentation might become necessary in children with congenital malformations or acquired diseases of the lower urinary tract. The commonly practiced surgical treatments, using gastric or intestinal mucosa, may induce severe, in particular metabolic, complications, due to the non-physiological interface of urine and the intestinal tissues. Tissue engineered functional bladder constructs may avoid these complications. The aim of this research was to study one component of such a construct, the in-vitro engineered stratified human urothelium. Its morphology, functionality and in particular its permeability properties were evaluated and the results compared to the data of native human urothelium.

Methods: Human urothelial cells, harvested from biopsies of children undergoing open bladder surgery were cultured in serum-free keratinocyte medium and urothelial stratification was induced altering the calcium concentration of the medium. Histology, immunohistochemical methods, and transmission as well as scanning electron microscopical studies assessed morphology and functional polarization of the engineered constructs. Permeability of the in vitro urothelial construct for water, urea, ammonia and protons was measured in modified "Ussing"-chambers. All the results were compared with the data of native urothelium, which normally acts as barrier to urine.

Results: As in native urothelium, the stratified human urothelial construct showed 3 to 4 cell layers showing a morphological polarity. It consisted of a basal membrane, basal, intermediate and superficial cells forming villosities and expressing glycoecys. Morphologically asymmetric apical cell membranes could be shown. Gap junctions, tight junctions and desmosomes were demonstrated at the lateral membrane junctions. Electron microscopy and immunohistochemistry using monoclonal antibodies against cytokeratins, integrins and cellular adhesion proteins could show these findings. Apart from the lack of uroplakin expression, typical for the terminal differentiation of superficial cells, the findings analyzing the urothelial constructs were comparable to the ones of native urothelium. Permeability measured and averaged (in cm/s) were to water, through urothelial constructs (9.77±0.54)x10⁻⁵ and through native human urothelium (7.71±0.75)x10⁻⁵; to urea, through urothelial constructs (4.05±0.32)x10⁻⁵ and through native human urothelium (4.92±0.69)x10⁻⁵; to ammonia, through urothelial constructs (6.20±0.40)x10⁻⁵ and through native human urothelium (7.00±1.01)x10⁻⁵. The results for proton permeability will also be presented.

Conclusion: Although, the in vitro engineered human stratified urothelial construct did not show complete terminal differentiation of its superficial cells, it was in all other functional aspects comparable to native human urothelium and in particular was characterized by similar permeability properties. This might render the in vitro urothelial construct, after being grown on a compliant degradable support alone or in co-culture with smooth muscle cells, suitable to facilitate bladder augmentation.

THE MICROBIOLOGY OF BLADDER AUGMENTATION IN CHILDREN

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Background: Many children with augmented bladders have urine which is colonized with bacteria but the nature of this colonization is poorly defined. We reviewed a large number of augmented children to identify the microbiology of their augmented bladders and the effects of antibiotic use in their urinary bacteria.

Methods: Consecutive patients (1990–96) were reviewed who underwent bladder augmentation with colon or ileum. We analyzed the records for two years after augmentation to define types of bacteria, antibiotic resistance patterns, and the effect of antibiotic use on these bacteria.

Results: Ninety-nine patients were identified, 54 boys and 45 girls. The most common diagnosis was myelomenigocele in 65%. All were on clean intermittent catheterization and 84 had adequate information to be included. Patients underwent an average of 4.6 urine cultures or 2.3 per year. Thirty-seven percent of all cultures were negative and 70% of all patients had a negative culture. Of the positive cultures, 30% grew E. coli, 15.3% grew Klebsiella, 8.3% grew Citrobacter, and 8.3% grew a Streptococcus species. Antibiotic sensitivity patterns revealed 19% of organisms to be pansensitive. The most common resistance (57%) was to penicillins, followed by cephalosporins in 40%, nitrofurantoin in 25%, and TMP-SMX in 21%. Only 6% were resistant to all oral antibiotics and none were panresistant. Fifty-five percent of patients use antibiotics and of these 74% use them intermittently. Antibiotic use did not significantly affect the number of negative cultures. Antibiotic use increased the risk of growing Citrobacter and Pseudomonas and lowered the risk of Enterobacter and Providencia. The use of antibiotics increased the number of bacteria resistant to TMP-SMX.

Conclusions: Most children with augmented bladders will have sterile urine at some time. E coli and Klebsiella were the most common organisms found in their urine. Resistance to commonly used antibiotics, TMP-SMX and nitrofurantoin, occurs in 25% or less. Antibiotic use did not significantly decrease the incidence of positive cultures but did result in an increase in the resistance to TMP-SMX.

LAPAROSCOPIC ACE (ANTEGRADE CONTINENCE ENEMA) IN SITU APPENDIX PROCEDURE FOR REFRACTORY CONSTIPATION AND FECAL INCONTINENCE IN CHILDREN WITH SPINA BIFIDA

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Background: The ACE procedure allows patients with neurogenic bowel to administer large volume enemas through a right lower quadrant stoma to flush their colons every other day. This results in freedom from refractory constipation and diarrhea required by unexpected episodes of fecal incontinence. We present a laparoscopic simplified technique using an unmodified in situ appendix.

Methods: 4 male and 4 female children (mean age 12, range 5 to 18) with neurogenic bowel underwent the ACE in situ appendix procedure. The procedure was done with laparoscopic assistance in association with other bladder and bladder outlet reconstructive surgery in 3 patients. In 1 patient, a purely laparoscopic ACE in situ appendix procedure was performed. The appendix and cecum are mobilized and the tip of the appendix was anastomosed directly to the skin of the right lower quadrant at one of the port sites. The cecum is fixed with a single suture to the posterior aspect of the anterior abdominal wall. The continence mechanism is simply a function of the length of the appendix and the mucosal coaptation of the appendiceal lumen. An 8-French silastic Foley catheter is used to stent the mucocutaneous anastomosis. Concomitant procedures included ileostomy, ileovesicostomy or sig-
were patients between Moldes Juan was surgery (50%). Mitrofanoff an continent necessary, a passive coaptation of the appendiceal lumen and use of small catheters allows for continued continence. The combined ACE and either ileovesicostomy or sigmovesicostomy procedures allow children to take control of their bowel and bladder evacuation programs.

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UMBILICUS RECONSTRUCTION IN PATIENTS WITH BLADDER EXSTROPHY

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Background and Purpose: We report our experience to improve the cosmetic aspect of the abdominal wall in exstrophic patients with a new technical procedure to reconstruct an umbilicus scar. If necessary, it can be combined with a simultaneous Mitrofanoff continent ostoma.

Methods: During the last four years, 6 male and 4 female (10) patients between 3 and 22 years old, with bladder extrophy were operated to perform a new umbilicus. The indication for surgery was cosmetic in all patients and was combined with a simultaneous Mitrofanoff continent ostoma with appendix in 5 patients (50%). The basic surgical technique consists in creation of a rectangular vascularised flap (2 X 4cm) of skin and subcutaneous tissue with a cephalic base in a previously selected place. The subcutaneous tissue is completely resected from the skin to facilitate folding and rotation. The distal side of the flap is rotated 360° to form a cylinder with the skin in the outside face that must be inverted with a stitch in the superior border and fixed to the rectus fascia or the proximal end of the appendix if a Mitrofanoff procedure is performed. Finally, the borders of the new umbilicus are fixed to the abdominal skin. A small gauze tampon is maintained into the umbilicus for 5-7 days to get a deep mucocutaneous anastomosis, avoid ectropion and improve the final cosmesis.

Results: No complication were related to the surgical procedure. All patients feel comfortable with their new umbilicus. The five patients with a Mitrofanoff ostoma catheterize easily. One patient had an small mucosal ectropion on the bottom of the umbilicus. No patient has required a surgical revision until now.

Conclusion: Umbilical reconstruction in exstrophic patients can be combined with any other surgical procedure because is short and simple. While primary goals in exstrophy patients is continence and absence of hydrenephrosis, this procedure is helpful to get a better cosmetic aspect of the abdominal wall and obtain a concealed and easily catheterizable Mitrofanoff ostoma.

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HOW WELL DO EXSTROPHY PATIENTS ACTUALLY VOID?

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Background: Achieving continence with preservation of renal function are goals in the care of patients with bladder extrophy. Young Dees Ledberter (YDL) bladder neck reconstruction should ideally provide continence and normal voiding dynamics without the need for intermittent catheterization. Herein, we review our experience with bladder neck reconstruction in this population with emphasis on voiding dynamics among those patients doing well.

Methods: We retrospectively analyzed our experience with all patients with extrophy-epispadias variant since 1992. We reviewed the staged reconstruction of these 24 children (17 classic bladder extrophy, 2 extrophy variants, 5 incontinent epispadias) excluding patients with additional neurogenic dysfunction. 19 patients (13 males, 6 females) have undergone complete reconstruction for continence. 6 patients who required bladder augmentation at the time of bladder neck reconstruction or thereafter are excluded along with 1 patient who underwent continent cutaneous diversion (29%). Subjective and objective data regarding voiding function and complications were collected.

Results: 13 patients (9 males, 4 females) have had YDL bladder neck reconstruction with 2 or more years follow-up (mean 4 years). 11 patients have dry intervals of at least 2 hours and are all felt by the parents to do well with voiding. Despite near or total subjective continence and "good" voiding, 8/11 (73%) of this subgroup have clinical problems related to emptying including recurrent urinary tract infections (5), epididymitis (2), and bladder calculi (2). Objective urodynamic findings confirm poor voiding in most patients after YDL. Findings include very slow flow rate (Qmax), high Valsalva pressure, and residual urine. These findings occur with both natural and maximal voiding effort.

Conclusion: Bladder neck reconstruction among extrophy patients can achieve continence without a necessity for intermittent catheterization. In our experience, patients who achieve these goals have an alarming frequency of clinical and urodynamic problems related to emptying. One must question the normalcy of the voiding pattern and the price to achieve continence among extrophy patients.

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AVOIDANCE OF INGUINAL INCISION IN CASES OF LAPAROSCOPICALLY CONFIRMED VANISHING TESTICLE SYNDROME

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Background: Non-palpable testicles may be due to the vanishing testicle syndrome, intraabdominal position, examination obscured by obesity or scar tissue, and rarely testicular agenesis. Laparoscopy provides an excellent means to distinguish these entities from each other without the need for an open abdominal exploration. We have investigated whether laparoscopy affects the need for an inguinal incision and exploration when no testicle is palpable, and the vas and vessels are seen to exit the internal inguinal ring laparoscopically.

Methods: Twenty children (mean age 54 months, range 8 to 186 months) were examined and found to have a non-palpable testis(s). There were 9 right, 10 left, and 1 pair of non-palpable testicles. The vanishing testicle syndrome was diagnosed laparo-
scopically: 1) vessels were seen exiting the external inguinal ring and no testicle was palpable despite an excellent examination under anesthesia, or 2) vessels were seen in the abdomen only with or without an intraabdominal testicular nubbin.

Results: Laparoscopy confirmed the vanishing testicle syndrome in 11 patients, intraabdominal testicles in 6 (1 bilateral), and 1 peeping testicle. An excellent examination under anesthesia was not possible in 2 patients with either obesity or previous inguinal surgery, and they underwent inguinal exploration after laparoscopy demonstrated vas and vessels exiting a closed internal inguinal ring. In the 11 cases of the vanishing testicle syndrome, 9 scrotal orchietomies with contralateral scrotal orchiopexies were performed through a median raphe incision. One ipsilateral inguinal hernia repair was performed with orchiectomy. One patient had laparoscopy only with blind ending vas and vessels seen in the abdomen but no identifiable nubbin. Intra-umbilical and median raphe incisions healed without obvious scars. Mean followup was 1 year.

Conclusions: When spermatic vessels are seen exiting the internal inguinal ring on laparoscopic examination in the setting of a non-palpable testicle, a median raphe scrotal incision can be used to remove the testicular nubbin, and also perform a contralateral orchiopexy if desired. Orchiectomy is possible through this median raphe incision even when the testicle is in the inguinal canal, as this distance in the young child is small. Cosmesis is excellent since one incision is within the umbilicus and the other on the median raphe of the scrotum.

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PELVIC-FRACTURE URETHRAL INJURIES IN FEMALE CHILDREN

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Background: Injuries to the female urethra associated with pelvic fracture are uncommon. Injuries may be partial or circumferential. When rupture has taken place at the proximal urethra is often total and complete and associated with vaginal laceration. The results of delayed surgical treatment to restore urethral continuity in girls with pelvic-fracture urethral disruptions were retrospectively reviewed.

Methods: Between 1984 and 1997, 6 girls 4 to 9 years old (median age 7) with urethral injuries associated with pelvic fracture were treated in our institution. Immediate treatment included suprapubic cystostomy in 2 patients, urethral catheter alignment and simultaneous suprapubic cystostomy in 3, and temporary urethral catheterization in 1. Of these 6 patients 4 with proximal urethral distraction defects were treated with delayed 1-stage anastomotic repair, 1 with mid urethral avulsion was managed by construction of a neourethra from the vaginal wall and 1 with a simple contusion did not require surgical treatment. Five patients had concomitant vaginal rupture and were treated at the time of the delayed urethral repair. Surgical approach was abdomino-vaginal in 2 cases and transpubic-vaginal in 3. Associated injuries also included rectal rupture in 3 and bladder neck laceration in 2. Overall postoperative follow-up ranged from 1 to 6 years (median 5).

Results: In all patients treated with suprapubic cystostomy alone and simultaneous urethral realignment and cystostomy urethral obliteration developed. The stricture-free rate of 1-stage anastomotic repair and substitution urethroplasty was 100%. One patient developed urinary incontinence while 1 other is only wet during night time. Retrospectively, associated bladder neck injury was related to the initial trauma in 1 of the 2 incontinent girls. Two recurrent vaginal strictures were treated successfully with additional transposition of lateral labial flaps.

Conclusions: In our study primary realignment of the urethra did not prevent the development of severe urethral obliteration. This study also emphasizes that the combined suprapubic-vaginal access is a reliable approach to reestablish urethral continuity and simultaneously reconstruct associated vaginal rupture or previous bladder neck damage.

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URETEROCELE DISPROPORTION (NON-OBSTRUCTIVE URETEROCELE) REVISITED

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Introduction: In most situations, an ectopic ureterocele is associated with hydroureteronephrosis of the upper pole of a double collecting system. We have previously described a clinical entity—non-obstructive ureterocele—in which an ectopic ureterocele exists without the typical ureteral and calyceal dilatation (J Urol 119:804, 1978) and called it ureterocele disproportion (UD) (Am J Radiol 152:567, 1989). Because the typical urographic and sonographic signs of an ectopic ureterocele are either subtle or absent, the presence of UD may be missed until the time of surgery. We reviewed our recent experience with UD.

Patients and Methods: We identified 18 patients (14 girls) with the diagnosis of UD treated at our hospital since 1986. Their ages at the time of presentation ranged from newborn to 5 years. Ten patients were evaluated because of prenatal hydroureteronephrosis. The remainder presented following urinary tract infection. All patients underwent sonography, voiding cystourethrography and excretory urography. UD was suspected when there was no visible upper pole (or no upper pole dilatation) in association with an ipsilateral ureterocele. In all patients, direct opacification of the ureterocele (accomplished at the time of surgery by puncture and injection of contrast agent) confirmed the diagnosis.

Results: All patients demonstrated vesicoureteral reflux into the ipsilateral lower pole. The appearance of the diminutive upper pole ureter ranged from a completely occluded "cord-like" structure to a non-dilated ureter connected to a tiny dysplastic upper pole. Four UD's were connected to upper pole multicystic dysplastic kidneys. Transurethral incision (TUI) of the ureterocele was the initial treatment in 10 patients, while ureterocele excision and common sheath ureteral reimplantation were performed as the initial treatment in seven. One asymptomatic patient has been followed without surgery for 4 years. In the TUI group, four had resolution of the lower pole reflux and required no further treatment, while six needed additional surgery to correct persistent lower pole reflux. No patient developed upper pole reflux after TUI. All patients who required secondary surgery after the initial TUI had other problems including paraureteral diverticulum (4), large ureterocele eversion (1), and poor renal function of the lower pole (1), whereas four patients who were successfully treated with TUI alone had only lower pole reflux.

Conclusions: The presence of ureterocele disproportion should be suspected when there is no visible upper pole (or no upper pole dilatation) in association with an ipsilateral ureterocele. Direct opacification of the ureterocele, easily accomplished at the time of cystoscopy, confirms the diagnosis. Upper urinary tract surgery is rarely required. In selected patients, endoscopic incision of the ureterocele may be an effective initial treatment, while in others additional surgery may be necessary to correct persistent lower pole reflux.

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THE USE OF COMPUTERIZED TOMOGRAPHY (CT) IN THE EVALUATION OF DUALIZATION ANOMALIES

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Background: In duplication anomalies the upper pole ureter has a greater chance for ectopia and obstruction. The upper pole is often markedly hydroureteric and dysplastic; the imaging
findings in these cases may result in the mistaken impression of
an upper pole cyst or cystic adrenal pathology. The radio-
graphic evaluation of children with duplication anomalies has
included excretory urography or sonography for evaluation of
the upper portion of the urinary tract and voiding cystography
for detection of reflux or other abnormalities of the lower
portion of the urinary tract. Scintigraphic studies are used to
quantitate renal function or for the visualization of the collect-
ing system in the presence of severe obstruction. However,
these conventional imaging studies often fail to delineate the
anatomy and quantitate upper pole function. We investigated
the role of spiral computed tomography as an adjunct in the
assessment of duplication anomalies.

Materials and Methods: Eight patients with duplication anom-
alias (6 ectopic ureters and 2 ureteroceles) were treated in the
period from January 1997 to December 1998. All patients were
evaluated with sonography, voiding cystourethrography and
Dimercaptosuccinic acid (DMSA) scans. In addition, all patients
underwent imaging of the abdomen and pelvis using a General
Electric Advantage High-speed scanner after the administration
of intravenous contrast. Plain films of the kidneys, ureters and
bladder (KUB) were obtained 15 minutes and 30 minutes after
the CT scan. All patients that have had surgery have had repeat
sonography and CT scan with contrast. Results of all imaging
studies, operative reports and pathologic specimens were
reviewed. The CT scan findings were correlated with both the
findings at surgery as well as the histologic findings. Function
is assessed by 1: quantitating Hounsfield units of both the
upper and lower poles of the duplicated kidney and 2: opacifica-
tion of the upper pole collecting system on delayed
KUB's.

Results: Six patients have undergone laparoscopic partial ne-
phrectomies with complete ureterectomies. One patient is
scheduled for an upper tract diversion and one patient was lost
to follow-up. There were six females and two males. The mean
age of patients is 4.3 months with a range of 2 weeks to 1.8
years. Six of the patients presented with antenatal hydrone-
phrosis and two with urinary tract infections. Only two of the
patients required sedation or analgesia for the CT study. Each
study takes an average of 3.0 minutes to complete. No child had
an adverse reaction from the contrast and all tolerated the
procedure well. The CT images beautifully depict the anatomy
with perfect accuracy. The site of termination of the ectopic
ureter could be seen in each case. The proximity of the upper
pole ureter to the lower pole ureter is nicely depicted which is
critical at the time of surgery. The amount of function of the
upper pole moiety seen on CT nicely correlates with the DMSA
findings as well as the histologic analysis of the nephrectomy
specimens. None of the patients with severe dysplasia and/or
no function on DMSA were seen to have contrast in the collect-
ing system on delayed KUB.

Conclusions: Our findings suggest that spiral CT with intra-
venous contrast followed by delayed plain films of the kidneys,
ureters and bladder is a powerful tool in the evaluation of
patients with duplication anomalies. The anatomy seen is
unparalleled by other imaging studies and there are no variables
in interpretation such as operator dependence that we see with
nuclear scans. It is easily and quickly performed and most of
the time does not require anesthesia. Spiral CT obviates the
need for nuclear scans and excretory urograms in patients with
duplication anomalies.

LOWER URINARY TRACT RECONSTRUCTION FOR NON-
FUNCTIONING RENAL MOIEITIES ASSOCIATED WITH
URETEROVESICAL JUNCTION PATHOLOGY: A REVIEW
OF THREE INSTITUTIONS' EXPERIENCE

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Background: The traditional treatment of non-functioning renal
segments associated with ureteroceles, ureteral ectopia, or ure-
tero vesical junction obstruction has been partial or total nephr-
tomy. Recent reports indicate that approximately fifty percent of
these patients treated with ablative upper tract surgery will re-
quire subsequent lower tract surgery. Due to the high incidence
of secondary bladder surgery in these patients, we present three
institutions' experience with initial lower urinary tract reconstruc-
tion with reimplantation of non-functioning renal moieties.

Methods: The medical records of twenty-four patients from
three different institutions were reviewed. The diagnosis of a
non-functioning renal segment was found during evaluation for
antenatal hydronephrosis (6), urinary tract infection (16), vaginal
discharge (1), and as a result of sibling screening (1). There were
22 girls and 2 boys that underwent lower urinary tract reconstruc-
tion for definitive management of non-functioning renal segments
at an average age of twenty-nine months. None of these patients
had upper tract surgery. Twenty-one patients had ureteral duplica-
tion and associated megaureters. All of these patients had tapering
of the non-functioning segment with common sheath reimplantations.
Three patients had primary megaureters associated with single
systems (all three were obstructing, two of these were also reflux-
ing) and were managed with tapering of the non-functioning
segment and reimplantation.

Results: All patients did well in the post-operative period. Fol-
low-up has ranged from 3 to 129 months (mean 37). Six patients were
found to have urinary tract infections at some point during follow-
up. Of these 6 patients, 4 had a single UTI (2 asymptomatic, one
dysuria, and one low grade temp), and the other two experienced
recurrent febrile UTI's. No patient has required an additional sur-
gical procedure or demonstrated a further decrease in renal function.

Conclusions: Primary lower urinary tract reconstruction in pa-
tients with non-functioning renal moieties associated with ure-
tero vesical junction pathology is safe, avoids upper tract surgery
and treats the obstructed or refluxing ureter definitively. Further
long term follow-up will be required to determine if this is the
preferred surgical therapy for management of patients with non-
functioning renal moieties.

COST AND OUTCOME TRENDS IN OPEN PYELOPLASTY:
A SINGLE INSTITUTION FIVE-YEAR REVIEW

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nessee.

Background: Recently reports of decreased costs and shortened
hospital stays associated with the surgical correction of an ob-
structed ureteropelvic junction have been published. These
improvements have been attributed to many recent trends in surgical
practice; such as, type of incision and other modifications in
surgical technique, advances in laparoscopic surgery, and surgical
pathways designed to increase efficiency on a cost and patient care
basis. We report our results of age- and disease-matched patients

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with regard to hospital and operating room costs, operative time, and length of hospitalization to better define the nature of these improvements and to uncover other areas of potential improvement.

Methods: A retrospective review of clinical and cost data from patients undergoing an open pyeloplasty via the flank approach between February 1994 and February 1999 was performed. Patients were grouped based upon age (> or < 18 months), those undergoing pyeloplasty alone, and those undergoing pyeloplasty with retrograde pyelography (RGP) alone. Comparisons were made between groups for the entire length of the review and within groups based upon the date of surgery (before or after September 1997). Data were obtained from hospital and clinic records and compared with the two-tailed t test.

Results: Pyeloplasty was performed in 108 children, there were no deaths and no complications requiring readmission within three days of the operation. Two patients required readmission within 30 days for complications related to the operation, and three patients required a revision secondary to recurrent obstruction for an overall success rate of 97.2%. Fifty-six patients were older than 18 months of age (mean 88.9 months, range 20-204 months) and 52 patients were less than 18 months of age (mean 4.3 months, range 1-17). There was no significant difference between length of hospitalization, total hospital charges, or ancillary hospital charges (radiology, anesthesiology, pharmacy or laboratory) between these two groups. However, mean operating room charges ($4138 vs. $3398, p = 0.0001) and mean operative time (140 minutes vs. 114 minutes, p = 0.008) were both significantly lower in the younger patient group. Thirty-two patients underwent pyeloplasty alone and 42 patients underwent pyeloplasty with RGP alone. As expected there was a significant difference in operating room charges ($4092 vs. $3223, p = 0.0001) and radiology charges ($143 vs. $23, p = 0.02) between these two groups. Interestingly, total hospital costs were also significantly lower in the pyeloplasty only group ($5386 vs. $4778, p = 0.04), as all ancillary hospital costs were lower. There was no difference in length of hospitalization between the groups. Of the 42 patients in the RGP group none had any abnormality which altered the planned surgical procedure. Seventy-three operations were performed prior to September 1997 and 35 afterwards. Mean length of hospitalization was 2.6 days in the earlier group and 2.2 thereafter. This difference approached statistical significance (p = 0.08).

Conclusion: Open pyeloplasty via the flank incision is a safe, efficient and effective treatment for ureteropelvic junction obstruction in patients of all ages. The lower operative time and charges in younger patients likely relates to the lower incidence of RGP in this group. This factor, in addition to the data from the pyeloplasty alone vs. pyeloplasty and RGP alone study arm, points to a large area of potential savings, especially since the information obtained from the RGP did not change the clinical or surgical course of any patient in our study. The trend towards shorter length of hospitalization has occurred despite no significant change in surgical technique or perioperative management, therefore it is felt that this has resulted from changes in general hospital and insurance company practices that as yet, have not affected morbidity and mortality outcomes.

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ISCHEMIA-REFUSION INJURY INDUCES RENAL TUBULAR CELL PRODUCTION OF TNF-α

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Background: Significant renal dysfunction and cellular injury can occur following short periods of renal ischemia. While the exact mechanisms of ischemia-reperfusion injury remain undefined, mediators of inflammation including TNF-α have been implicated in the pathogenesis of this injury. Traditionally, infiltrating macrophage have been considered the primary source of renal TNF-α. We conducted the following animal studies to determine whether early renal ischemia-reperfusion injury induces TNF-α production, and if so, whether TNF-α production following this stimulus is localized to resident renal cells or infiltrating macrophage.

Methods: Male Sprague-Dawley rats were anesthetized and exposed to various periods of renal ischemia, with or without reperfusion. Sham operated animals served as negative controls, while animals exposed to 0.5 mg/kg ip lipopolysaccharide (LPS = endotoxin), a potent inflammatory stimulant, served as positive controls. The kidneys were harvested following different time intervals of ischemia and reperfusion. TNF-α mRNA content (RT-PCR), TNF-α protein expression (ELISA), and TNF-α bioactivity (WEHI-164 cell clone cytotoxicity assay) were determined. The cellular localization of TNF-α was evaluated using immunohistochemistry.

Results: Renal TNF-α mRNA was induced after 30 minutes of isolated ischemia. While sham treated animals expressed low levels of TNF-α (19 ± 1.1 pg/gm protein), TNF-α levels were significantly increased following 1 hour of ischemia and 2 hours of reperfusion (48 ± 13 pg/gm protein, p < 0.05). Similarly, TNF-α bioactivity, measured with the cytotoxicity assay, peaked following one hour of ischemia and 2 hours of reperfusion (11 ± 2.4 U/mg protein, p < 0.05, vs. sham = 2.3 ± 0.9 U/mg protein). TNF-α production following ischemia-reperfusion injury localized primarily to renal tubular epithelial cells. In contrast, animals exposed to LPS demonstrated a primarily glomerular distribution of TNF-α production.

Conclusion: Ischemia-reperfusion injury induces renal tubular cells to produce TNF-α. The cellular localization of TNF-α production appears to be injury specific, i.e. renal tubular cells are the primary source of TNF-α following an ischemic insult, whereas LPS induces glomerular TNF-α production. As the role of TNF-α in renal ischemia-reperfusion injury becomes defined, the development of an anti-TNF therapy, which attenuates ischemia-reperfusion induced renal injury, may become a realistic clinical possibility.

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A MODIFIED EXTRAPEVICAL URETERAL REIMPLANTATION TECHNIQUE USING AN "INVERTED-Y" DURSOS DISSECTION

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Background: Extravesical ureteral reimplantation has classically been performed with a detrusor dissection involving full mobilization of the ureterovesical junction (UVJ) until the ureter is attached only by the bladder mucosa. The UVJ is then advanced distally, and a distal ureteral anchoring stitch is used to prevent prolapse of the ureter out of the detrusor tunnel. As an alternative simplified approach, detrusor dissection can be performed in the shape of an inverted-Y, mobilizing only the proximal and lateral aspects of the UVJ, leaving the distal trigonal and detrusor attachments intact. The UVJ remains at the original position in this technique, anchored in place by its natural distal attachments, obviating the need for a distal anchoring stitch. It was the objective of this project to assess the merits and outcome of the "inverted-Y" detrusor dissection.

Methods: From July 1997 to April 1999, 18 unilateral and 16 bilateral extravesical ureteral reimplantations (50 ureters) were performed using the inverted-Y detrusor dissection, employing
either a laparoscopic approach or an open incision. All patients were monitored prospectively. Voiding efficiency was assessed by uroflowmetry and ultrasound post-void residual volume measurements at 2 days, 2 weeks and 2 months post-operatively. Upper tract imaging and voiding cystourethrogram were obtained 2 months post-operatively, and renal ultrasound was performed at 1 year.

Results: Satisfactory kink-free extravesical ureteral reimplantations were achieved in all 50 ureters using the inverted-Y detrusor dissection. All ureters remained well anchored in their natural positions using this technique, without requiring a distal ureteral anchoring stitch. The inverted-Y detrusor dissection was technically simple to perform, and was less time consuming. Follow-up to date demonstrates no post-operative ureteral obstruction (100% patency), and persistent reflux was seen in only one ureter (98% reflux resolution). Urethral catheters were successfully removed 1 or 2 days post-operatively with no urinary retention noted. Voiding efficiency using the inverted-Y technique compares favorably to reported series, where a 4 to 21% rate of post-operative urinary retention has been reported in extravesical bilateral ureteral reimplantations (p = 0.036).

Conclusions: The inverted-Y detrusor dissection maintained a high rate of successful outcome (100% patency, 98% reflux resolution), comparable to the traditional techniques. The inverted-Y technique has the added advantages of being easy to perform, less time consuming, and obviating the risk of ureteral obstruction associated with the placement of a distal ureteral anchoring stitch. There was a statistically significant improvement in post-operative voiding efficiency, presumably due to decreased disruption in trigonal innervation. Our data suggest that the inverted-Y technique is an effective improvement over the traditional circumferential UVJ mobilization in extravesical ureteral reimplantations.

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DOUBLE ONLAY PREPUTIAL FLAP FOR HYPOSPADIAS REPAIR: EXPERIENCE WITH A NEW TECHNIQUE IN 46 PATIENTS.

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Background: Severe hypospadias can be reliably and safely repaired in one stage using island flaps of preputial skin. Problems with conventional technique however, include anastomotic strictures, penile asymmetry, and at times doubtful viability of the Byars flaps. Some of these problems can be resolved using the double onlay preputial flap for hypospadias repair as described by us (J. Urol. 156:832, 1996).

Methods: We reviewed the records of 46 children who underwent one-stage double onlay preputial flap hypospadias repair between June 1994 and July 1998. Patient age ranged from 6 months to 9 years (mean 12.2 months). Hypospadias was midshaft in 12 (26%), penoscrotal in 29 (63%), and perineal in 5 (11%) patients. The mean distance between the urethral meatus and the tip of the penis was 28mm (range 10–40mm). Chordee repair required dorsal plication in 29 patients. In 7 of these an additional ventral incision of the tunica albuginea and tunica vaginalis autograft with preservation of the urethral plate was needed to complete the repair. Pre-operative testosterone enanthate was given to 17 patients. Scrotal transposition was performed at the time of hypospadias repair in 9 patients.

Results: Mean follow-up was 15.2 months (range 3–47 months). Complications requiring reoperation occurred in 10 patients (21%). Seven (15%) boys developed fistulae. Of these six had perineal and one penoscrotal hypospadias. Fistula closure was required in all patients. A diverticulum developed in four (8%) patients. Two patients (4%) experienced meatal recession. Persistent penile curvature requiring repeat dorsal plication occurred in 2 patients (4%). One patient required revision for a bulky ventral skin strip. There were no complications in the 12 patients with midshaft hypospadias.

Conclusion: The double onlay preputial flap technique for hypospadias repair offers good cosmetic and functional results. Given the high incidence of penoscrotal and perineal hypospadias (74%) in our series, complication rates are comparable or better to those of other techniques.

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LONG-TERM EVALUATION OF HYPOSPADIAS REPAIR: PATIENT AND FAMILY PERSPECTIVE OF FUNCTIONAL AND AESTHETIC RESULTS

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Background: Multiple techniques have been developed for the management of hypospadias. Excellent cosmetic and functional results are now obtainable in most patients with the use of single stage repairs performed as an outpatient procedure. Determination of success in hypospadias repair should be based on how the cosmetic and functional results are perceived by the patient and his family. This study attempted to determine patient/family satisfaction with hypospadias repair.

Methods: A questionnaire listing various functional and aesthetic criteria was sent to 167 patients/families. Ninety-one (55%) responses were obtained following a single mailing. The first half of the questionnaire addressed functional concerns, and the second half addressed aesthetic concerns. Responses were analyzed to determine patient and parental satisfaction with every aspect of hypospadias reconstruction.

Results: Responses were obtained from patients/families 2–25 years following hypospadias repair (mean = 5.88 years). Functional criteria: 68 respondents answered all 5 questions relating to functional aspects of hypospadias repair (ability to void and direct urinary stream and have normal erections). Seventy-five percent of these respondents indicated complete satisfaction (51/68) with repair. Twenty-three patients did not answer all five questions. Four of these patients also had functional concerns. Overall 23% of respondents had functional concerns (21/91). The most common functional concern was urine spraying noted in 10 patients. Aesthetic concerns: 67 respondents answered all 7 questions regarding aesthetic aspects of hypospadias repair (overall appearance, penile bending, scarring and abnormal hair growth), 89.6% (60/67) of respondents indicated normal penile appearance, however only 50.7% were completely satisfied with every aspect of the aesthetic appearance. The most commonly noted concern was scarring on the ventral aspect of the penis along the suture lines. If all aspects of hypospadias repair were considered 53% of respondents indicated complete satisfaction.

Conclusions: Improvements in surgical techniques and instrumentation have improved the surgical reconstruction of hypospadias. Patient and familial satisfaction is primary in the determination of success in any genital reconstruction. Aspects that may appear minor can be a source of great concern for boys with hypospadias and their families. Identifying and managing these concerns will enhance management of this frequently noted malformation.

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FREE GRAFTS FOR PENILE CURVATURE

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Background: Patients with extensive penile chordee may require placement of a free graft to create a straight phallus. We reviewed our experience in patients undergoing primary (no previous surgery) and secondary repair using dermal and tunica vaginalis grafts for correction of penile chordee.

Methods: Between 1992 and 1998, 28 patients required placement of a free graft to correct penile chordee. Eight patients (29%), mean age 12 months, underwent primary repair using tunica vaginalis in 2 and a dermal graft in 6. Twenty patients (71%) required secondary repair due to recurrent chordee with or without hypospadias. Tunica vaginalis was used in 3 patients and dermal grafts were used in 17. Grafts were used if straightening did not occur after degloving of the penile shaft, dorsal plication and urethral plate division. Mean follow-up was 2 years.

Results: Residual chordee developed in 1 of 8 patients after primary repair and in 2 of 20 patients after secondary repair. All patients with residual chordee had tunica vaginalis grafts placed at the time of repair. There were no recurrences of chordee following dermal graft placement.

Conclusions: Conventional techniques such as penile degloving and dorsal plication can be used in most patients to correct penile chordee. Free grafts are more likely to be needed in patients requiring secondary repair. We believe the use of dermal grafts resulted in a successful repair compared to tunica vaginalis grafts which seem to have a higher incidence of residual chordee.

BOVINE PERICARDIUM AS A CORPORAL Cavernosal Patch Material in the Repair of Penile Chordee

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Background: In the treatment of penile chordee involving significant intrinsic disproportion in corporeal dimensions, two alternative methods of repair include plication of the convex side, versus the release and patching of the concave side. In using the release and patch approach, it would be desirable to have a biocompatible patch material which is readily available. Bovine pericardial graft is available off-the-shelf, has a texture similar to tunica albuginea, and may be a suitable material for the patching of corporeal cavernosal defects. It was the objective of this project to assess the outcome of using bovine pericardial graft in the repair of penile chordee.

Methods: Of the 50 patients who underwent hypospadias / chordee repairs between January 1997 and February 1999, 12 were found to have significant chordee (>30° curvature) secondary to corporeal disproportion not amenable to aggressive release of skin, scar tissue, and or/urethral tethering. These patients had a median age of 3 years (range 10 months to 10.5 years). With full mobilization of the urethra off the corpora cavernosa, repair was achieved by performing a transverse releasing incision on the concave aspect of the corporeal bodies. The resulting corporeal cavernosal defect was then covered by the application of an elliptical patch of bovine pericardium.

Results: With a mean follow-up of 16 months (range 4 to 25 months), none of the 12 patients had evidence of recurrent or residual chordee. A single bovine pericardial patch was used in 10 patients; one patient required 2 patches and another required 3 patches. The longitudinal dimension of the bovine pericardial patches used had a mean value of 11 mm (range 4 to 23 mm), which on average corresponded to approximately 20% of the child’s stretched penile length (range 10 to 69%). The bovine pericardial graft was generally well tolerated by all patients. One patient extruded a patch per urethra 6 months post-operatively, but nevertheless maintains straight erections at 16 months follow up.

Conclusion: Repair of chordee using bovine pericardial patch is generally well tolerated, and is associated with satisfactory results. Bovine pericardium is readily available off-the-shelf, obviating the added morbidity associated with the harvesting of patch material from autologous donor sites. In our experience, equivalent straightening of chordee using the alternative plication technique would have resulted in an unacceptably large degree of penile shortening in the majority of the patients (up to 69% of stretched penile length). Our experience supports that the repair of penile chordee using bovine pericardial patch is an effective technique, with the added benefit that post-operative penile length is maximized compared to the plication technique.

RING AROUND THE PENIS: A TECHNIQUE TO CORRECT SEVERE HYPOSPADIAS AND LOWER THE RISK OF URETHRAL STRICTURE OR MEATAL STENOSIS, INITIAL RESULTS

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Background: Complication free repair of severe hypospadias still presents a daunting challenge to the reconstructive surgeon. Duckett’s transverse island (TI) is the procedure most commonly used to correct these anomalies but both published outcomes and our own experience with the TI suggests that the complication rates are still significant. We designed a procedure to correct severe hypospadias with the objective of trying to avoid postoperative urethral strictures and meatal stenosis, which we find the most vexing of the early postoperative complications.

Methods: The penile incisions used to fashion the neourethra in this procedure take the shape of a ring around the glans. During the course of tissue mobilization, full access to the corporeal bodies is provided for chordee correction. After chordee release, the ring of shaft and preputial skin which surrounds the glans is split in the dorsal midline creating two strips of tissue which are transposed on their pedicles around their respective sides of the penis to the ventrum. The pedicles require relatively limited mobilization so the blood supply to the tissue seems quite reliable. Because the pedicles lay on opposite sides of the penis, they afford the penile shaft a symmetric appearance and avoid any tendency to torsion caused by a single pedicle. The two transposed skin strips are sutured together in the ventral midline to create a rectangular sheet of tissue which is then tubularized to form the neourethra. This technique of neourethral configuration avoids a circumferential anastomosis.

Results: This procedure has recently been performed in 10 patients with severe hypospadias. Only one patient developed a meatal stenosis and no urethral strictures occurred.

Conclusion: The “ring around the penis” technique to repair severe hypospadias employs well vascularized tissue flaps which require minimal mobilization and the neourethral closure avoids a circumferential anastomosis. The technique has allowed us to correct severe hypospadias with a lower risk of meatal stenosis or urethral stricture and additionally it offers some cosmetic advantages over the standard procedures for severe hypospadias. Technical aspects of the procedure will be discussed.

HYPOSPADIAS FAILURE: OUTCOME OF URETHRAL RECONSTRUCTION 36 PATIENTS

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Background: The authors present their experience regarding the evaluation and treatment of 36 patients with failed hypospadias repair. All the cases required one or more substantial surgical procedures for the urethral reconstruction. Patients presenting with minor complications (small fistulas, diverticulum, meatal stenosis) were excluded from the present study.
Methods: Between January 92 and December 97, 36 patients underwent a major urethral reconstruction for failed hypospadias. Three groups of patients were identified:

1. partial (21 cases) or complete dehiscence (4 cases) of the nec-urethra.
2. urethral stenosis (6 cases) requiring surgical revision and un treatable conservatively.
3. multiple fistulas (5 cases) requiring partial or complete urethral reconstruction. A free graft was used in 19 cases: 17 buccal mucosa (1 tubularized, 16 onlays), 1 tubularized bladder mucosa and extra-genital skin in one case. In 7 cases an onlay was performed using the residual preputial/penile skin. In 4 cases the Snodgrass technique was employed and in 3 cases advancement of the distal urethra was achieved through wide mobilization of the entire urethra. Finally, in 3 cases a two-stage reconstruction was selected.

Results: The mean follow-up has been of 30 months a uroflowmetry and US scan to evaluate the post-void residual was done in 2/3 of the patients and was normal. In 26 cases a complete correction was achieved after the first operation. In 7 cases further surgical procedures were required due to complications: 6 patients developed a urethral stricture after a buccal mucosa graft. In one case receiving preputial onlay a urethral diverticulum appeared. One of the six patient presenting urethral stenosis had a fistula. Three patients are waiting for another procedure (2 Brackas + 1 failure). No major complications were found, at the moment, in the patients treated by urethral advancement or Snodgrass technique.

Conclusion: In many cases of failed hypospadias repair the resulting deformities are significantly worse than the presenting congenital anomaly. The following surgical reconstruction requires sophisticated technical solutions and, at the same time, a clear pre-operative planning and a flexible intra-operative approach. Buccal mucosa free graft represent at the present time the most valuable alternative for urethral substitution. Even for these complex forms an excellent success rate can be expected but a long-term follow up is mandatory for a complete evaluation and before any final judgement.

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MANAGEMENT OF RECALCITRANT AND FULMINANT VENEREAL WART INFECTIONS IN CHILDREN WITH HIGH DOSE CIMETIDINE

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Background: Perigenital warts can be a very distressing and difficult problem to treat in children. At times repetitive treatment with locally applied caustic agents are necessary, other times treatment of perigenital warts necessitates the use of general anesthesia and multiple operative procedures to eradicate the problem. Cimetidine an H2 receptor antagonist which has been used mainly to treat peptic ulcer disease has been reported to be useful in the treatment of mucocutaneous candidiasis, herpes simplex, herpes zoster and verruca because of it's immunomodulatory effects. There are several published studies indicating it's efficacy in treating warts in non-genital areas.

Methods: We treated 4 children, 3 girls and 1 boy, ranging in age from 10 months to 34 months. Two girls were treated with Cimetidine (300mg/kg/day in 3 divided doses) as adjunctive therapy after laser fulguration of large numbers of perineal, peri vaginal and perianal lesions. There girls could not be rendered wart free because of the extensive nature of the problem. Attempting to fulgurate all warts would have left them with large areas denuded and burned by the laser treatment. A staged approach was taken in these children, with the idea to retreat areas in 1-2 months if adjunctive treatment did not work. One boy and one girl were treated primarily with Cimetidine (300 mg/kg/day in 3 divided doses).

Results: The first 2 girls had no additional verruca formation after their laser fulgurations with the adjunctive cimetidine treatments. The boy and girl treated primarily were rendered wart free after 3 months of treatment with no surgical or caustic agents to treat the warts.

Conclusion: It is apparent that cimetidine treatment of venereal warts is a safe and effective means of managing this very difficult problem in children. There were no complications associated with the treatment and all patients tolerated the medication without any difficulties. It has become our preferred means of managing numerous venereal warts in children of all ages.

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UROPLAKIN AND ANDROGEN RECEPTOR EXPRESSION IN THE HUMAN FETAL FEMALE GENITAL TRACT: INSIGHTS INTO THE DEVELOPMENT OF THE VAGINA IN NORMAL FEMALES AND IN CONGENITAL ADRENAL HYPERPLASIA

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Background: The development of the vagina remains under debate. Although a dual origin of the vagina has been popularized, other theories support a Mullerian duct (MD) or wolffian (WD) origin or various combinations of these structures and the urogenital sinus (UGS). UPs are specialized membrane proteins of the urothelial plaque constituting the asymmetrical unit mem-}

brane of the bladder and represent specific molecular markers of urothelial differentiation. Recently, immunohistochemical detection of uroplakins (UPs) has been available. We hypothesize that the epithelium of the dorsal wall of the UGS involved in the formation of the sinovaginal bulbs (SVB) will express UPs. In addition, the localization of the androgen receptor (AR) and its temporal expression during development may, in part, explain the varied effects of androgens on the lower female genital tract in CAH (CAH).

Methods: Lower GU tracts were obtained from 4 human female fetuses ranging in gestational age from 9-18 weeks. Each of the 4 specimens were serially sagittally-sectioned. Representative sections were stained with hematoxylin and eosin (H and E), rabbit antibodies against pan-uroplakin (UP), previously reported in adult bladder and ureteral urothelium (AJP 147:1383, 1995), and antibodies to the AR.

Results: At 9 weeks, the WDs and the paired MDs were present. The UGS showed evidence of evagination and the formation of the SVBs. The urothelium of the entire UGS expressed UPs including the region of the dorsal wall involved in evagination and formation of the SVBs. These 2 discrete regions of the UGS were not directly in contact with the MD or WD. At 12 weeks, the SVBs show squamous epithelialization and the Mullerian ducts are lined with columnar epithelium. ARs are expressed as early as 9 weeks in the epithelium and the stroma of the UGS, SVB, MDs and the WDs. By 14 weeks, AR expression is almost absent in the urothelium of the UGS and the epithelium of the lower vagina and MDs. The AR expression in the stroma surrounding these structures was also diminished.

Conclusions: We have shown that the area of evagination of the UGS expresses UPs and is involved in the formation the SVBs which differentiate into the lower vagina by 18 weeks. This further substantiates the UGS origin of the lower vagina. Since testosterone (T) is known to inhibit the formation of the lower vagina, the timing of the exposure to systemic testosterone in CAH will determine the phenotypic appearance of the external genitalia and the effect of T on the development of the lower genital tract. Clinically, if exposure to T occurs after 12 weeks, only clitoral hypertrophy occurs. Since AR is absent in the urothelium of the UGS and the epithelium of the vagina and the MD by 14 weeks, this may suggest that the tissues are no longer androgen-sensitive.
after that critical time and vaginal development will proceed normally.

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CONSENSUS ON THE APPROACH TO ANTENATALLY DETECTED UREOLOGIC ABNORMALITIES

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Background: A genitourinary abnormality is detected antenatally in approximately 1% of pregnancies. Pediatric urologists are increasingly becoming involved in decisions regarding antenatal intervention (AI). Currently, there are no written guidelines when AI is indicated. A survey of pediatric urologists was undertaken to evaluate current practice patterns and recommendations regarding AI.

Materials and Methods: A two-sided survey instrument was mailed to all members of the Society for Fetal Urology (SFU). The survey included 7 case scenarios that addressed critical decision points in patients with antenatally detected GU abnormalities. A second mailing was sent to initial non-responders. All data was tabulated at one center. A chi-square analysis was used for statistical analysis.

Results: A total of 112 of 188(60%) members (99 North American, 13 Non-North American) completed the survey. The first two case scenarios involved near term fetuses with fetal lung maturity: There was almost uniform agreement in delaying intervention for a 32 week fetus with a suspected UPJ obstruction (99%). For a 36 week fetus with suspected PUV without oligohydramnios most respondents (69%) elected no intervention while a minority would have induced early delivery (27%). When comparing (NA) to (AI) respondents, 46% of NNA would have induced early delivery compared to 26% of NA. (p-value = .01) Three cases involved fetuses with low to normal amniotic fluid without fetal lung maturity: Most respondents (86%) recommended serial ultrasounds to follow an 18-week fetus with suspected PUV when amniotic fluid was normal but decreasing. Almost all respondents agreed with some type of AI for a 28 week fetus with a solitary kidney and a suspected UPJ (76% renal shunt, 13% induce delivery as soon as lung maturity, 6% aspirate left renal pelvis now, 6% aspirate left renal pelvis prior to delivery). Most respondents agreed with no intervention (55% serial ultrasounds, 27% no intervention) for a 20 week fetus with suspected bilateral renal cystic disease. Finally, two cases involved scenarios with lung immaturity and available bladder and/or renal electrolytes: For a 23-week-old fetus with suspected PUV and oligohydramnios with normal bladder electrolytes, most respondents agreed with some form of AI (71% vesicoamniotic shunt, 7% serial aspiration, 7% amnioinfusion). For a 20 week fetus with suspected PUV, oligohydramnios and renal and bladder electrolytes indicating a non-functioning right kidney, there was no clear consensus with 55% favoring AI (47% vesicoamniotic shunt, 5% serial aspirations, 3% right pelvis shunt) and 38% recommending no AI because of anticipated fetal demise.

Conclusion: There is a general consensus among pediatric urologists regarding AI for specific GU abnormalities. Intervention is indicated by this group in cases with proven renal function and oligohydramnios with fetal viability. In cases with normal amniotic fluid AI is not recommended by a majority of practitioners regardless of the detected abnormality. There is a trend favoring early delivery of fetuses with severe GU abnormalities and proven lung maturity even in the absence of oligohydramnios.

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OUTCOME ANALYSIS OF VESICOAMNIOTIC SHUNT INSERTION FOR SUSPECTED BLADDER OUTLET OBSTRUCTION

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Background: Antenatal detection of obstructive uropathy is widely utilized, and vesicoamniotic shunting is an accepted procedure in well-defined instances. Few data have been presented on the risks and benefits of these procedures. We present a consecutive case series from a coordinated antenatal/postnatal treatment program on the outcome of vesicoamniotic shunting procedures.

Methods: Over a five year period (93–98) eighty-two patients were seen with suspected bladder outlet obstruction in an antenatal high-risk obstetrical unit. The multidisciplinary antenatal high risk unit included a pediatric urologist. A prospective protocol included vesicoamniotic shunting for fetuses with bilateral hydronephrosis, large bladders, and oligohydramnios. Following delivery, infants were treated at an adjacent children’s hospital, and outcomes were determined with respect to pulmonary, renal and bladder function. These results were correlated with antenatal urine electrolytes, and antenatal renal ultrasonography.

Results: Over a 5 yr. period, five fetuses underwent vesicoamniotic shunting for oligohydramnios. One additional fetus received a shunt at 23 wks. gestational age, because of decreasing amniotic fluid combined with a multicystic kidney, and suspected evolution of cystic etiology in the second kidney. All shunts were placed between 20 and 28 weeks. None of the antenatal procedures were associated with precipitous labour. Amniotic fluid was restored in 5, and all bladders were successfully drained. Two fetuses extruded the shunts and had multiple sequential shunts placed. All six fetuses were delivered at term. One died shortly following birth with pulmonary insufficiency. One had gastrochisis at the site of the shunt. Five survived and of these, three had severe renal insufficiency and two had mild renal impairment. Underlying diagnoses at birth included posterior urethral valves (n=3) prune belly syndrome (1) and urinary tract atresia (2). Prenatal urinary electrolytes did not correlate with the degree of eventual renal impairment.

Conclusion: Although vesicoamniotic shunting is effective in reversing oligohydramnios, it is variable in its ability to achieve sustainable good renal function in infancy. No specific antenatal parameters were effective in predicting eventual good renal function. Pulmonary function cannot be assured with restoration of amniotic fluid.