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UROLOGICAL SURVEY

SECTION EDITOR

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EDITORIAL COMITTEE

PATHOLOGY

Dedifferentiation of prostate cancer grade with time in men followed expectantly for stage T1c disease

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J Urol, 166: 1688-1691, 2001

Purpose: To assess whether the Gleason grade changes in men followed expectantly with clinical stage T1c prostate cancer.

Material and Methods: Were studied 70 men with stage T1c prostate cancer who underwent watchful waiting with repeat needle biopsy sampling to assess for progression. After the initial cancer diagnosis all men had at least 1 other biopsy demonstrating cancer. The mean age of the 70 patients was 64.5 years (range 52 to 74), the mean serum PSA level at the initial diagnosis was 5.6 ng/ml and the percent-free serum PSA values available in 64 men averaged 17.3%.

Results: Of 70 cases 9 (12.9%) showed a significant change in grade from Gleason scores 6 or less to 7 or greater. The average follow up of those patients without a change in grade was 22 months and greater than those with a change in grade. There was no difference between the groups with and without changes in grade in regard to initial prostate specific antigen (PSA), percent-free PSA, or PSA density or velocity. Of 9 cases there were 5 (56%) and 8 (89%) with grade change that occurred at 12 and 15 months or less after initial biopsy, respectively. In contrast, only 1 of 24 (4%) patients in whom last re-biopsy was performed 24 months or greater after the initial cancer diagnosis had a change in grade.

Conclusions: Because most grade changes occurred relatively soon after biopsy, it implies that tumor grade did not evolve but rather the higher grade component was not initially sampled. During a 1 and half to 2-year period after biopsy there is no evidence that prostate cancer grade worsens significantly. Men with prostate cancer need not feel concerned about waiting several months before undergoing surgery after biopsy. Furthermore, men undergoing watchful waiting can be assured that there is little evidence that prostate cancer grade worsens during the short term.

Editorial Comment

Due to screening for prostate cancer, a higher number of patients each year are diagnosed having stage T1c disease. In cases of insignificant disease according to criteria proposed by Epstein (J Urol, 160: 2407-2411, 1998), watchful waiting may be considered. Insignificant disease relates only to volume of tumor found in patients submitted to radical prostatectomy. There is a probability of 94.4% for the tumor to have a volume of less than 0.5 cc. It does not refer, however, whether the particular tumor will behave as a latent or clinical carcinoma. Epidemiologically, there is a higher probability for the tumor to behave as a latent one. The findings of this paper are in accordance with the epidemiological data. The patients without a change in grade probably harbor latent cancers; however, they were studied in a relatively short period (22 months of follow up, in average). For the therapeutic approach in clinical stage T1c, age of the patient is critical in the decision for surgical intervention or watchful waiting. This dilemma will remain until an individual marker discloses individually the biological behavior of the prostate cancer.

Dr. Athanase Billis

IMAGING

MR angiography and preoperative evaluation for laparoscopic donor nephrectomy

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AJR, 178: 1489-1495, 2002

Objective: The purpose of our study was to evaluate the effectiveness of gadolinium-enhanced MR imaging in imaging arterial, venous, and ureteric anatomy in a group of potential laparoscopic renal donors and to compare our findings with those established at surgery.

Subjects and Methods: Sixty-four consecutive patients underwent successful laparoscopic donor nephrectomy. Imaging of the kidneys was performed before surgery with MR imaging and breath-hold three-dimensional gadolinium-enhanced MR angiography. All studies were reviewed prospectively by one of two attending radiologists. Results were compared with findings at the time of laparoscopic nephrectomy.

Results: Of the 64 patients, MR imaging and MR angiography identified 30 patients with normal arterial, venous, and ureteric anatomy, and concordance was found at surgery in 29 of these patients. Vascular anomalies were depicted on MR imaging in 34 patients, with complete concordance at surgery in 29 patients. The use of MR angiography for revealing arterial anomalies had a sensitivity of 89.4%, specificity of 94.1%, and accuracy of 90.6%. For venous anomalies, there was a sensitivity of 98.3%, specificity of 100%, and accuracy of 98.4%. No important ureteric anomalies were identified at surgery or on MR imaging.

Conclusion: Renal MR imaging and gadolinium-enhanced MR angiography provide a safe, accurate, and minimally invasive means of comprehensive assessment of the potential living renal donor.

Editorial Comment

Multiple imaging modalities have been used for the preoperative evaluation of renal donors, including ultrasound, CT, nuclear medicine, excretory urography, and angiography. Digital angiography with subtraction is still considered the gold-standard test, but is invasive. Recently two minimally invasive methods, CT angiography and MR angiography have been used as alternative techniques for preoperative radiologic evaluation of renal donors. Recent studies with gadolinium-enhanced MR angiography have established it as an accurate imaging modality for the visualization and evaluation of patients with clinical suspicion of renovascular hypertension, patients candidates to partial nephrectomy, and living renal donors for open nephrectomy. This study evaluated 64 consecutive potential laparoscopic renal donors which had conventional MR imaging of the kidneys and gadolinium-enhanced MR angiography .The radiologic findings for each renal donor were correlated with surgical findings. MR angiography proved to be very useful tool for the detection of arterial and venous anomalies (accuracy of 90.6% and of 98.4%, respectively). This study emphasizes the utility of the recently developed techniques of contrast-enhanced MR angiography such as the breath-hold three-dimensional gradient-echo sequence and the utilization of maximum-intensity-projection and volume rendering imaging. With this technique each renal vessel is particularly evaluated. With this method all the main and accessories renal arteries were well demonstrated. For the detection of renal artery stenosis involving 50% and 75% of its lumen, volume rendering imaging has been shown to have a positive predictive value of 95 % and 90% while the maximum-intensity-projection technique had a positive predictive value of 86% and 68% respectively (1).

MR angiography and CT angiography (2) are far superior for preoperative evaluation of living renal donors in comparison with excretory urography and conventional angiography. Both methods are better to demonstrate small renal stones, venous and ureteral anomalies and small renal tumors. CT-angiography is

particularly useful for the evaluation and detection of renal artery aneurysms, particularly those calcified. Calcified renal artery aneurysms are very difficult to evaluate with MR angiography.

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Dr. Adilson Prando

Noncontrast computed tomography in obstructive anuria: a prospective study

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Urology, 59: 861-864, 2002

Objectives: To evaluate the role of noncontrast computed tomography (NCCT) in the determination of the cause of obstructive anuria and to compare its accuracy with that of the traditional methods of combined plain abdominal x-ray (KUB) and gray-scale abdominal ultrasonography (US).

Methods: The study included 40 consecutive patients with obstructive anuria. In addition to the routine evaluation, which included history, clinical examination, biochemical profile, KUB, and US, all patients underwent NCCT. The study patients were tested against an age and sex-matched control group that included the normal contralateral kidneys of 57 consecutive patients who underwent KUB, US, and NCCT for acute flank pain during the same study period. The reference standard for the determination of the cause of obstruction was retrograde or antegrade ureterography with or without ureteroscopy or open surgery. The absence of obstruction in the control group was confirmed by nonequivocal normal intravenous urography of the side free of flank pain. Both NCCT and combined KUB and US were compared regarding the sensitivity, specificity, and overall accuracy.

Results: The study group had 48 renal units, because obstruction was bilateral in 8 patients and of a solitary kidney in 32. Of the 42 renal units with calculus obstruction, the site of stone impaction was identified in all renal units by NCCT (sensitivity 100%) and in only 25 by combined KUB and US (sensitivity 59.5%)—a significant difference ($p = 0.0001$). Of the 6 renal units with noncalcular obstruction, both NCCT and US diagnosed the cause of obstruction in 3. The overall sensitivity of NCCT in the determination of the cause of obstructive anuria was 94% and that of combined KUB and US was 58%—a significant difference ($p = 0.0001$). The specificity of NCCT was not significantly different from that of combined KUB and US (96.5% versus 93%, respectively). The overall accuracy of NCCT was 95% and that of combined KUB and US was 77%—a significant difference ($p = 0.0003$).

Conclusions: In patients with obstructive anuria, conventional KUB and US could not identify the cause of ureteral obstruction in about 40% of the patients. Under such conditions, NCCT can accurately provide the diagnosis, obviating the need of invasive and expensive diagnostic procedures.

Editorial Comment

Most commonly, in the emergency setting, the cause of obstructive anuria could not be diagnosed by routine examinations (plain x-ray and ultrasonography), and invasive techniques such as retrograde pyelography or percutaneous nephrostomy must be employed to achieve diagnosis. During the last 7 years, noncontrast CT has been used for evaluation of renal colic with high sensitivity and specificity. Based on the previous success of this method for diagnosing the cause of renal colic, the authors assessed whether noncontrast CT could be useful in evaluation of obstructive anuria. The inclusion criteria were no urine for 24 hours or longer, serum creatinine greater than 2 mg/dL, and at least one kidney with preserved parenchyma.

The authors found that the obstruction was bilateral in 8 patients and of a solitary kidney in 32. Lithiasis was the cause of obstruction in 42 renal units (87.5%). Noncalcular obstruction was caused by ureteral stricture in 3, ureteropelvic junction obstruction in 1, and by advanced bladder tumor invading both ureters in 2 renal units. Treatment was decided according to the nature of the obstructing lesion and included relief of the obstruction either immediately or after a period of initial drainage using a ureteral catheter or percutaneous nephrostomy tube.

Diagnosis of obstructive anuria due to stone disease could not be confidently made on the basis of the plain abdominal x-ray, since its sensitivity in detecting ureteral calculi ranges from 45% to 59%. Moreover, suspicion and even evidence of an abdominal calculus on x-ray is not assurance that the calcification is in the urinary tract. Ultrasonography can accurately diagnose urinary tract obstruction, however it is of limited value for diagnosing the cause of obstruction, which is of utmost importance in the emergency setting, for decision on how to relief the obstruction. In the present series, combined plain x-ray film and ultrasound failed to diagnose the cause of anuria in 40.5% of the cases with calculous, and in 50% of the noncalcular cases.

When available, noncontrast CT can accurately provide the diagnosis of obstructive anuria in the emergency setting, and therefore must replace the invasive imaging examinations such as retrograde and antegrade pyelography, as well as diagnostic ureteroscopy.

Dr. Francisco J.B. Sampaio

HUMAN REPRODUCTION

Can varicocelectomy significantly change the way couples use assisted reproductive technologies?

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J Urol, 167: 1749-1752, 2002

Purpose: We assessed how varicocelectomy alters semen quality in a large cohort of infertile men and determined whether it can change patient candidacy for assisted reproductive technology procedures.

Materials and Methods: A cohort of 540 infertile men with clinical palpable varicocele underwent microsurgical varicocelectomy and were followed more than 1 and 2 years postoperatively for alterations in semen quality and conception, respectively. Preoperatively and postoperatively the total motile sperm count was calculated in all semen analyses. Based on total motile sperm count values patients were divided into 4 groups according to the type of assisted reproductive technology for which they qualified, including 0 to 1.5 million or less (intracytoplasmic sperm injection candidates), 1.5 to 5 million or less (in vitro fertilization

candidates), 5 to less than 20 million (intrauterine insemination candidates) and 20 million or greater sperm (spontaneous pregnancy candidates). Preoperative and postoperative semen quality was compared among individuals in these cohorts to determine the shifts in assisted reproductive technology care that are possible after varicocelectomy.

Results: Mean patient age was 29.5 years (range 18 to 58). Microsurgical varicocelectomy was bilateral in 393 patients (73%), on the left side in 146 (27%) and on the right side in 1 (0.2%). A positive response to varicocelectomy, defined as a greater than 50% increase in total motile sperm count, was observed in 271 patients (50%). An overall spontaneous pregnancy rate of 36.6% was achieved after varicocelectomy with a mean time to conception of 7 months (range 1 to 19). Of preoperative in vitro fertilization and intracytoplasmic sperm injection candidates 31% became intrauterine insemination or spontaneous pregnancy candidates after varicocelectomy. Of intrauterine insemination candidates 42% gained the potential for spontaneous pregnancy.

Conclusions: Varicocelectomy has significant potential not only to obviate the need for assisted reproductive technology, but also to down stage or shift the level of assisted reproductive technology needed to bypass male factor infertility.

Editorial Comment

Varicocele is the most common cause of male infertility, according to the World Health Organization. It affects 15% of all male population and 40% of men presenting abnormalities on semen analysis. The real role of this treatment in male infertility has been discussed for quite a long time. It is known that conventional surgical approaches lead to a recurrence rate of 15% to 30%, due to the fact that there are collateral veins, mainly from the cremasteric, that are not treated by the conventional surgical treatment modalities.

The present study was firstly presented at the 2001 AUA annual meeting, and it is now published. It brings important practical information for the urologist, gynecologist and reproductive specialist. First, the treatment was performed by microsurgery. It is known that the recurrence rate after microsurgical varicocele ligation is only 1%. Second, it is important to note that 73% of the varicocele patients had bilateral varicoceles. This incidence is higher than reported by most published books and papers. However, according to our personal experience, we also believe that the majority of varicoceles are bilateral. Therefore, the urologist must have great care during the patient physical examination. Third, this is the first study, to my knowledge, to demonstrate that the indication for assisted reproduction can chance after varicocele treatment. This finding has economic and medical impact, since costs associated with intrauterine insemination are significantly lower as compared to the ones of in vitro fertilization and intracytoplasmic sperm injection. In addition, intrauterine insemination and spontaneous pregnancy are associated with very low multiparity rates, which occur in 30% of all high complexity assisted reproductive technologies. Multiparity is associated with potential significant perinatal morbidity.

Dr. Sandro C. Esteves

The risk of major birth defects after intracytoplasmic sperm injection and in vitro fertilization

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N Engl J Med, 346: 725-730, 2002

Background: It is not known whether infants conceived with use of intracytoplasmic sperm injection or in vitro fertilization have a higher risk of birth defects than infants conceived naturally.

Methods: We obtained data from three registries in Western Australia on births, births after assisted conception, and major birth defects in infants born between 1993 and 1997. We assessed the prevalence of major birth defects diagnosed by one year of age in infants conceived naturally or with use of intracytoplasmic sperm injection or in vitro fertilization.

Results: Twenty-six of the 301 infants conceived with intracytoplasmic sperm injection (8.6 percent) and 75 of the 837 infants conceived with in vitro fertilization (9.0 percent) had a major birth defect diagnosed by one year of age, as compared with 168 of the 4000 naturally conceived infants (4.2 percent; $p < 0.001$ for the comparison between either type of technology and natural conception). As compared with natural conception, the odds ratio for a major birth defect by one year of age, after adjustment for maternal age and parity, the sex of the infant, and correlation between siblings, was 2.0 (95 percent confidence interval, 1.3 to 3.2) with intracytoplasmic sperm injection, and 2.0 (95 percent confidence interval, 1.5 to 2.9) with in vitro fertilization. Infants conceived with use of assisted reproductive technology were more likely than naturally conceived infants to have multiple major defects and to have chromosomal and musculoskeletal defects.

Conclusions: Infants conceived with use of intracytoplasmic sperm injection or in vitro fertilization have twice as high a risk of a major birth defect as naturally conceived infants.

Editorial Comment

High complexity assisted reproduction, especially intracytoplasmic sperm injection (ICSI), drastically changed the treatment of severe male infertility. It offers a real possibility of paternity for men who were previously named sterile. However, many questions are being discussed as to the future impact of this technology to the offspring.

The results of the present study are alarming, although others have reported no increase in genetic abnormalities between ICSI patients and the normal population (1). In spite of that, the high risk for birth defects reported by this study emphasizes the need for proper indication and counseling before treatment initiation.

The results of the present study suggest that the injection of the spermatozoa inside the oocyte, by a microinjection needle, does not offer additional damage, since the odds ratio for birth defects were similar between ICSI and in vitro fertilization (IVF). IVF does not use microinjection. It seems that the increase in birth defects may be related to the treatment group. Many ICSI cases are performed in couples whose infertility etiology has a genetic origin in the male partner. One of these examples is non-obstructive azoospermia. In a recent study, Palermo et al. (2) performed chromosomal analysis of epididymal and testicular sperm in azoospermic patients undergoing ICSI. They found an overall aneuploidy rate of 11.4% in men with non-obstructive azoospermia, which was significantly higher ($p = 0.0001$) than the 1.8% detected in epididymal sperm from men with obstructive azoospermia and also the 1.5% found in ejaculated sperm. These findings reinforce the hypothesis that the increase in birth defects is more likely to be related to the group of the patients treated by the technique, and not to the technique itself. Along the same lines, the musculoskeletal defects may be related to the associated-multiparity perinatal morbidity. However, future studies will help to clarify and understand many unsolved questions.

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Dr. Sandro C. Esteves

PEDIATRIC UROLOGY

Urologic injuries associated with repair of anorectal malformations in male patients

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J Pediatr Surg, 37: 339-344, 2002

Background/Purpose: Serious injuries to the urinary tract may occur during the repair of an anorectal malformation, especially in boys. This review of a large series of patients characterizes factors that may either lead to, or prevent, those injuries.

Methods: A retrospective review of 1,003 boys with anorectal malformations was performed.

Results: A total of 129 injuries in 1,003 patients were identified. Five hundred seventy-two of the 1,003 patients (group A) underwent definitive repair at the authors' institution. In this group, there were 19 urologic injuries; 1 bladder perforation, 1 divided ureter, 2 divided vas deferens, 1 prostatic injury, 7 seminal vesicles were opened and closed, and in 7 cases, the urethra was opened and closed during the repair. Follow-up ranges from 15 years to 1 month and no late sequelae have been observed. The second group (B) consisted of 431 patients who underwent various operations at other institutions. In this group, 110 urologic injuries in 97 patients were noted. These included neurogenic bladder (n= 27), persistent, recurrent or acquired recto-urethral fistulae (n= 30), posterior urethral diverticulae that required reoperation (n= 23), urethral injuries leading to stenosis or acquired atresia (n= 19), pull-through of major urinary structures (n= 2), injured ureter (n= 1), opened seminal vesicle (n= 1), divided vas deferens (n= 4), impotence (n= 1), and loss of ejaculation (n= 2). Several significant associations were noted. The most significant was that all 27 patients with neurogenic bladder and all 19 of those in group B with urethral injuries did not undergo a distal colostogram to define the level of the fistula before repair. Posterior urethral diverticulae were seen only in cases of recto-bulbar urethral fistulae repaired via an abdominal-perineal approach.

Conclusions: Significant urologic injuries are associated with the repair of anorectal malformations. The risk of injury is increased in those patients who undergo repair without a distal colostogram.

Editorial Comment

Most boys born with anorectal malformations have a fistula between the rectum and the urinary tract. Repair of these defects necessarily involves the separation of these two systems, and therefore this generates a significant risk of injury to important urogenital structures. The authors' overall results were 12.9% of injuries to the urogenital system.

It is interesting to note that the posterior-sagittal anorectoplasty and its variants do not affect lower urinary tract function unless surgical techniques are combined with major transabdominal procedures and extensive retrovesical dissection. This conclusion is based on the fact that no postoperative neurogenic bladder was found when the patient was not submitted to a retrovesical dissection.

Urethral injuries are 100% preventable. Except in cases of recto-perineal fistulas, the repair never should be performed without a preoperative distal colostogram. There is a significant risk of urologic injury during the repair of an anorectal malformation in a male patient. The posterior sagittal approach, if performed without a preoperative distal colostogram, has a significantly higher risk than other surgical approaches.

Dr. E. Alexsandro da Silva

Vesicoureteral reflux: a new treatment algorithm

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Curr Urol Rep, 3: 107-114, 2002

Vesicoureteral reflux (VUR) affects about 1% of all children and carries an increased risk of pyelonephritis and long-term renal impairment. There are several approaches to the treatment of VUR: antibiotic prophylaxis (conservative treatment), open surgery, and endoscopic treatment. For many patients, endoscopic treatment cures VUR with a single procedure, eliminating the need for long-term antibiotic treatment and avoiding the trauma of a major surgical procedure. The choice of material for endoscopic treatment is of key importance, and, until recently, all available materials were associated with concerns regarding safety and efficacy. Emerging data demonstrate that dextranomer/hyaluronic acid (Dx/HA) copolymer has good long-term safety and efficacy in treating VUR. A new treatment algorithm is, therefore, proposed, recommending that most children with persistent VUR (longer than 1 year) be offered endoscopic treatment with Dx/HA copolymer as an alternative to prolonged antibiotic prophylaxis or open surgery.

Editorial Comment

The present paper focuses on a very actual issue, as evidenced by the vesicoureteral reflux (VUR) highlights in the last American Urological Association meeting. VUR treatment depends on the grade of reflux, patient age and the presence of kidney injury. Currently, decrease of morbidity is the main role of endoscopic treatment.

The major problem with this kind of therapy is the choice of the material for endoscopic treatment. The material may have the following characteristic: a) to maintain its volume at the injection place for a long time b) to be biological compatible and no immunogenic c) to be no oncogenic d) do not present migration e) to be cheap and obtained easily. Several materials were used to this purpose (1): polytetrafluorethylen (PTFE, Teflon), micro implants of silicon (Macroplastique), collagen, alcoholic polyvinyl, injected bioglass, Deflux system, and autologous agents (fat, collagen, chondrocyte, bladder muscle cell).

In the present paper, the authors showed that the endoscopic treatment of VUR with dextranomer/hyaluronic acid copolymers presented good result, and propose an algorithm to the VUR treatment, highlighting the endoscopic treatment. However, there is no consensus about the best material to the endoscopic treatment of VUR and therefore, careful consideration on the endoscopic treatment must be taken.

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Dr. Luciano A. Favorito

RECONSTRUCTIVE UROLOGY

Long-term voiding pattern of patients with ileal orthotopic bladder substitutes

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Purpose: Good long-term functional outcome of orthotopic bladder substitution will ultimately decide whether it is here to stay. Therefore, we analyzed exclusively voiding patterns of long-term survivors with an orthotopic ileal bladder substitute.

Materials and Methods: In all patients with an ileal orthotopic bladder substitute day and nighttime continence status, voiding frequency, bladder capacity and pad usage were prospectively assessed by frequency volume charts and a standardized questionnaire. All men surviving 5 or more years with a median follow up of 95 months (range 60-132) were evaluated.

Results: Spontaneous voiding was possible in 82 of 86 (95.3%) evaluated patients after catheter removal. Daytime continence increased from 61% after 3 months to 92% at 12 months and remained stable throughout the following 4 years yet decreased slightly thereafter. Nocturnal continence rates were 10% to 15% lower throughout the study period. Functional reservoir capacity averaged 473 ml. after 12 months and did not change in subsequent years. After a decrease during the first 12 months, daytime frequency (4.1 to 4.8 times daily) and nocturia (1.8 to 2.3 a night) did not change in the next decade. Patient age at surgery was an important determinant for long-term reservoir capacity, nocturia and continence status.

Conclusions: These data provide evidence for good long-term functional outcome following orthotopic ileal bladder substitution up to 11 years. We attribute the sustained ability to void to the relatively small reservoir size, which is made of 40 to 44 cm. of ileum, the avoidance of any funnel shaped outlet but rather a side-to-end intestine-urethral anastomosis as well as lifelong meticulous follow up.

Editorial Comment

When measuring quality of life in patients with orthotopic bladder substitution functional voiding is the most important factor. Day and nighttime urinary incontinence, urethral or anastomotic strictures as well as failure to empty the bladder substitute requiring intermittent or permanent catheterization may divert substantially from any perceived quality of life advantage of orthotopic bladder reconstruction. Continence and voiding function following orthotopic bladder substitution are determined primarily by characteristics of the reservoir and a preserved, innervated outlet mechanism.

The authors presented 83 patients who lived at least 5 years with the bladder substitute. In their series daytime continence rates averaged at 92% at 12 months and remained stable for 4 years. However, it must be stressed that their good functional results and the high patient acceptance were favorably influenced by careful patient selection. They did not perform this type of urinary diversion in patients with poor general health, not able or willing to participate in lifelong careful follow up and not able to learn a new voiding pattern postoperatively.

Satisfactorily long-term functional outcome requires efficient patient selection, minimally traumatic surgery to the sphincter area, preservation of maximal urethral length and urethral innervation, a low pressure reservoir, and meticulous postoperative surveillance and repeated voiding instructions. Appropriate follow up by a well-informed urologist is more important than the surgery itself to ensure good results.

Dr. E. Alexsandro da Silva

Male perineogenital anatomy and clinical applications in genital reconstructions and male-to-female sex reassignment surgery

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Plast Reconstr Surg, 109: 1301-1310, 2002

To determine the possibility of providing alternative surgical techniques for male genital reconstruction and for male-to-female sex reassignment surgery, the authors undertook an anatomic investigation of the perineogenital region in male cadavers. Anatomic dissection was performed on 14 male adult human cadavers (fresh and formalin-preserved) studying the main afferent vessels to the anterior perineal region and their mean internal diameters: deep external pudendal artery (0.60 mm), superficial perineal artery (0.50 mm), and funicular artery (0.37 mm). We established their exact topography, together with vascular anatomic variations, main vascular anastomosis circuits (base of the penis, scrotal septum, and perineal fat and lateral spermatic-scrotal fascia), angiosomes, anatomy of the rectovesical septum cavity, and their "critical" key points of dissection. The authors discuss the clinical possibility of elevation of a "tree" of previously described paragenital-genital flaps including mainly those based on the terminal branches of the internal pudendal vascular system, the erectile tissue pedicled flaps, and finally, flaps of the external pudendal system. The authors indicate the concrete vascularization system for each flap.

Editorial Comment

The anatomy of the perineum and the genitals has been well described in classic treatises, although recent studies of its cutaneous vascularization system have been decisive for enhancement of genital reconstructive surgery. During the past two decades, the internal pudendal artery and its terminal branches have possibly been the most frequent objects of investigation, and many different perineal axial flaps have been used for reconstruction of congenital malformations, for acquired genital defects, and for sex reassignment surgery.

The main afferent vessels to the skin of the genitals and the anterior perineal region in the male anatomy are the anterior scrotal arteries, which are direct branches from the femoral vascular system; and the posterior scrotal arteries, which are terminal branches of the superficial perineal vessels from the internal iliac vascular system. In addition, there is another vascular structure that is relevant in this field, the funicular artery, a proximal branch of the inferior deep epigastric artery from the external iliac system. The authors are congratulated to perform an elegant and practical study. As a result of their anatomic study of the cutaneous angiosomes of the anterior perineal region in human male cadavers, they described several logical clinical applications of flaps based on the internal and external pudendal system.

Dr. E. Alexsandro da Silva

INVESTIGATIVE UROLOGY

Decreased sperm number and motile activity on the f1 offspring maternally exposed to butyl p-hydroxybenzoic acid (butyl paraben)

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Butyl p-hydroxybenzoic acid (butyl paraben, BP) is widely used as a preservative in food and cosmetic products. Routledge et al. showed that BP is weakly estrogenic in both in vitro and in vivo (rat uterotrophic) analyses. We investigated whether maternal exposures to BP during gestation and lactation periods affected the development of the reproductive organs of the F1 offspring. Pregnant Sprague-Dawley rats were injected

subcutaneously with 100 or 200 mg/kg of BP from gestation day (GD) 6 to postnatal day (PND) 20. In the group exposed to 200 mg/kg of BP, the proportion of pups born alive and the proportion of pups surviving to weaning were decreased. The body weights of female offspring were significantly decreased at PND 49. The weights of testes, seminal vesicles and prostate glands were significantly decreased in rats exposed to 100 mg/kg of BP on PND 49. In contrast, the weights of female reproductive organs were not affected by BP. The sperm count and the sperm motile activity in the epididymis were significantly decreased at doses of 100 and 200 mg/kg of BP. In accordance with the sperm count in the epididymis, the number of round spermatides and elongated spermatides in the seminiferous tubule (stage VII) were significantly decreased by BP. Testicular expression of estrogen receptor (ER)-alpha and ER-beta mRNA was significantly increased in 200 mg/kg of BP treated group at PND 90. Taken together, these results indicated that maternal exposure of BP might have adverse effects on the F1 male offspring.

Editorial Comment

Maternal events during pregnancy and lactation may cause important problems on the offspring, and sometimes theses problems are permanent. Dietetic and hormonal treatments are some maternal events that can produce malfunction on endocrine and reproductive organs.

This paper evaluates the effect of food and cosmetic products containing estrogen on the offspring. Sometimes, food and cosmetic products can be used with no information on their composition and side effects. The authors have used simple method (i.e., body weight), and molecular biology to evaluate the mRNA expression of alpha and beta estrogen receptors, and they showed that the maternal exposure to butyl paraben, which is widely used as a preservative agent, can cause several effects on reproductive organs of the male offspring. This is a very important issue, mainly because that, in the vast majority of the cases, these effects just will appear at puberty or at the beginning of the reproductive life. At that time, besides a correct diagnosis about etiology is difficult, the chance of treatment and reversion of these alterations are decreased.

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Successful transplantation of three tissue-engineered cell types using capsule induction technique and fibrin glue as a delivery vehicle

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Recent advances in cell biology and tissue engineering have used various delivery vehicles for transplanting varying cell cultures with limited success. These techniques are frequently complicated by tissue necrosis, infection, and reabsorption. The purpose of this study was to investigate whether urothelium cells, tracheal epithelial cells, and preadipocytes cultured in vitro could be successfully transplanted onto a prefabricated capsule surface by using fibrin glue as a delivery vehicle, with the ultimate goal for use in reconstruction. In the first step of the animal study, tissue specimens (bladder urothelium, tracheal epithelial cells, epididymal fat pad) were harvested for in vitro cell culturing, and a silicone block was implanted subcutaneously or within the anterior rectus sheath to induce capsule formation. After 6 to 10 days, when primary cultures were confluent, the animals were re-anesthetized, the newly formed capsule pouches were incised, and the suspensions of cultured urothelia cells (n = 40), tracheal epithelial cells (n = 32), and preadipocytes (n = 40) were implanted onto the capsule surface in two groups, one using standard culture medium as a delivery vehicle and the second

using fibrin glue. Histologic sections were taken, and different histomorphologic studies were performed according to tissue type. Consistently in all animals, a highly vascularized capsule was induced by the silicon material. In all animals in which the authors used fibrin glue as a delivery vehicle, they could demonstrate a successful reimplantation of cultured urothelium cells, tracheal epithelial cells, or preadipocytes. Their animal studies showed that capsule induction in combination with fibrin glue as a delivery vehicle is a successful model for transplantation of different in vivo cultured tissue types.

Editorial Comment

In clinical situations with limited availability of intact urothelium, autologous urothelial cells grown and expanded *in vitro* using tissue engineering methods are an alternative source for reconstructive urologic surgery in the genitourinary tract. Previously the use of urothelial cells as a single-cell suspension in fibrin has been successfully performed to regenerate differentiated epithelium *in viv*o (1).

In tissue engineering, donor tissue is dissociated into individual cells or small tissue fragments, expanded in culture, and either reimplanted into the autologous host after attachment to an appropriate matrix *in vitro* or directly implanted *in vivo* using a supportive transport matrix. Implanted silicone materials can induce a capsule formation in a specific shape with a strong neovascularization providing a favorable environment for the transplanted urothelial cells (1, 2). For practical application, tissue engineering approaches can be categorized into more substitutive approaches, where the aim is the *ex vivo* construction of a living tissue or organ similar to a transplant, versus histeoconductive or histeoinductive concepts. The latter approach corresponds to the authors' concept of tissue engineering approach in the present paper, which has the advantage that there is no need of an intrinsic vascular system for parenchymal cell survival.

Fibrin glue supports the attachment of the transplanted cells to the capsule surface, enhances the migration capacity of the cells, allows the diffusion of growth and nutrition factors, and is a nutrient medium itself. These properties are important features for reimplantation of cells until revascularization and definitive incorporation occur. Thus, the fibrin glue serves not only as a mechanical carrier and delivery system for cell transplantation, but offers essential additional biological properties.

This experimental approach combines the considerable *in vitro* expansion capacity of graftable cells with the advantages of transplanting an actively proliferating single-cell suspension in an appropriate biological carrier system. A similar principle could also be used to epithelialize the lumen in bladder or ureter reconstruction, as well in urethroplasty. However, for those approaches, the reconstruction of a smooth muscle cell layer or corpus spongiosum would be required.

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