# Letters

## Are there long-term effects of extracorporeal shockwave lithotripsy in paediatric patients?

Sir,

The authors have described very well the long-term consequences of extracorporeal shockwave lithotripsy (ESWL) in children and concluded that there was no effect of ESWL on renal growth or development of hypertension or diabetes mellitus later in life [1].

Although, not USA Food and Drug Administration approved, ESWL is a commonly used treatment option for paediatric stone disease [2]. The long-term bio-effects of ESWL are still considered controversial, especially in the paediatric population.

Various studies have been conducted in this regard, but the dilemma persists as to whether ESWL given in the early decades of life is harmful as regards the later development of hypertension, diabetes mellitus or impact on renal growth. These issues are of concern as several animal studies have proved the potential for adverse long-term consequences of ESWL in the paediatric population in the form of a significant decrease in effective renal plasma flow or a significant increase in mean arterial blood pressure [3]. These animal studies suggest that the acute renal injury may progress to scar formation resulting in loss of functional renal volume. Also in a 9-year follow-up study of children, overall renal size was found to be decreased not only in the treated kidney after a session of ESWL, but also in the contralateral normal kidney [4].

There is ample published evidence that suggests the development of new onset of diastolic hypertension in adults long after lithotripsy and the paediatric kidney is more susceptible to injury as compared with adults [5].

Nevertheless, there is the utmost need for further research with longer follow-up durations on the mechanism and consequences of shockwave renal injury, especially in young populations.

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## Reply

Sir,

Extracorporeal shockwave lithotripsy (SWL) is the most commonly used treatment for non-complex urinary calculi in adults. In pediatric patients, there were concerns about the possible harmful effects of ESWL on the parenchyma of growing kidneys. These concerns were assessed in animal models. Kaji et al. [1] reported histological changes in renal tubular and glomerular epithelium and interstitial cells in immature rabbits after SWL. These changes were thought to be the cause of an increase in arterial blood pressure among tested rabbits. However, SWL in that study was delivered directly to the renal parenchyma, which is different from clinical practice where SWL is delivered to the stones. Moreover, Kaji et al. [1] noticed no significant reduction in renal function or renal growth after SWL in immature rabbits.

On the other hand, clinical studies have proved that there are no significant long-term harmful effects of SWL on pediatric kidneys [2–3] and SWL did not statistically affect linear growth (body height) or renal function in the pediatric population [4].

The concerns about the development of systemic diseases, e.g. hypertension and diabetes, were studied in adults with contradictory results. In pediatric patients, Lottmann et al. [2] and Frick et al. [3] found that SWL was not associated

with increased incidence of hypertension. Our study proved the long-term safety of SWL for renal stones during childhood because there were no harmful effects on renal growth, linear growth or development of hypertension or diabetes [5].

The lesson learnt from these studies is that safe application of SWL in children requires adequate targeting, low energies and a limited number of shocks per session for sparing the renal parenchyma any possible deleterious effects [2]. Although SWL was considered to be the method of choice for managing renal stones in children of all ages [6], more studies with long-term follow-up are required to confirm the safety of SWL in pediatric patients.

**Ahmed R. EL-Nahas**

*On behalf of the authors*

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## *De novo* erectile dysfunction after anterior urethroplasty: a systematic review and meta-analysis

Sir,

We read this article [1] with interest regarding the incidence of *de novo* erectile dysfunction (ED) after anterior urethroplasty. The authors have tried to clear the 'grey areas' in anterior urethroplasty and ED. However, the authors need to address some issues. We would like to know the basis by which the authors calculated the incidence of ED, as no clear cut universal definition for ED was followed in the different studies. Of a total 36 studies, preoperative data about ED was only available in five studies [457 patients (≈20%) out of the total 2323], so how did the authors calculate that some patients developed *de novo* ED, as their preoperative status was unknown. It also needs to be clarified at what time after surgery erectile function was assessed and how the authors concluded that there was a 1% incidence of ED. Moreover, the total number of patients with ED was 165, which is 7.1 % of the total 2323 patients.

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## Reference

1 **Blaschko SD, Sanford MT, Cinman NM, McAninch JW, Breyer BN.** *De novo* erectile dysfunction after anterior urethroplasty: a systematic review and meta-analysis. *BJU Int* 2013 [Epub ahead of print] DOI: 10.1111/j.1464-410X.2012.11741

## Reply

Sir,

We appreciate the opportunity to provide additional information about our article [1]. The questions you raise point out some limitations of meta-analysis in general. In this study, meta-analysis involves comparing studies with heterogeneous definitions of erectile dysfunction (ED) and variation in follow-up duration across studies.

The definition for ED differed across studies and ranged from new reports of ED postoperatively to a decline in International Index of Erectile Function (IIEF) score. Whether or not ED was self-reported, if all patients were questioned about ED, or if a standardised questionnaire to evaluate ED was used, is described for each study in Table 1. In retrospective studies where patients were not asked about erectile function in advance, new onset ED after urethroplasty is self-reported and is subject to recall bias. In meta-analysis, the most weight was given to studies that prospectively questioned all patients about ED with a standardised questionnaire.

The time frame by which ED was determined was not provided in the methods for all studies included in our meta-analysis. The prospective studies that evaluated ED typically used a time frame of 6–18 months to evaluate postoperative erectile function. The study follow-up time frame is listed in Table 1.

 

Random effects meta-analysis was used to calculate the incidence of ED rather than simply dividing the number of cases of ED by the total number of patients [2].

**Sarah D. Blaschko and Benjamin N. Breyer**

*On behalf of the authors*

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## Newer and novel artificial urinary sphincters (AUS): the development of alternatives to the current AUS device

Sir,

Despite the growing emergence of mini-invasive surgical treatments for urinary incontinence (i.e., urethral slings, injections of bulking agents, adjustable continence therapies, and stem cell therapies), the AMS 800® artificial urinary sphincter (AUS) (American Medical Systems, Minnetonka, MN, USA) has remained the 'gold standard' treatment for stress urinary incontinence in men and women over the last 40 years. Despite the favourable outcome and satisfaction rates after its implantation, this device continues to be associated with the risk of local complications (i.e., atrophy, erosion and infection) or mechanical failure. Thus, regular revisions and/or explantations are mandatory in at least 30% of AUS devices. New and more sophisticated AUS devices have recently been developed to improve function, occlusive efficiency, and biocompatibility relative to its current design.

In a recent article, Chung et al. [1] provided a review of new and/or innovative AUS devices.

The FlowSecure AUS (FlowSecure™, RBM-Med) was designed in 1991 with early functional outcomes reported in 2006. It has the main advantage of instantly increasing the pressure delivered to the urethra, only during stress increases in intra-abdominal pressure. When deactivated, the cuff returns to the initial low pressure level, never exceeding 40 $cmH_2O$, thus minimising the risk of urethral atrophy and/or erosion. As indicated by Chung et al. [1], despite encouraging preliminary results with the FlowSecure™, more recent data have shown high mechanical failure and infection rates, as well as risk of pump assembly perforation in short- to intermediate-term follow-up.

The Periurethral Constrictor (Silimed, Rio de Janeiro, Brazil) was released in 1996. It is simple to use and of low cost. However, there are only a few published studies with controversial outcomes for the device in a post-prostatectomy urinary incontinence setting [2]. The routine use of this device is debatable.

The Tape Mechanical Occlusive Device (GT Urological LLC, Minneapolis, MN, USA) is a non-hydraulic one-piece device that is manually controlled by the patient through its on/off buttons [3]. It has been implanted in dogs to assess its function, occlusive efficiency, and biocompatibility and in human male cadavers to assess its occlusive efficiency and sizing, with encouraging results. Prospective clinical studies are awaited.

Two additional devices have been developed in France. The ZSI 375 (Zephyr Surgical Implants, France) was released in 2005 (http://zephyr-si.com/zephyr/index.php?lg=en.) and has not yet been approved by the French Health Authority Agency (http://www.has-sante.fr/portail/jcms/c_896387/zsi-375-cnedimts-du-24-novembre-2009-2254) despite publication of recent data. No strong basic (bench and animal) and/or clinical data are available, and the use of this device should be done under a prospective controlled study before extensive use. Indeed, only a few preliminary monocentric retrospective observational studies have been reported. There are no favourable comparisons with the AMS 800®, and as opposed to the two following devices, the Versatile Automated Device and electromechanical device, it has not followed, at least through published papers, the usual process of validation.

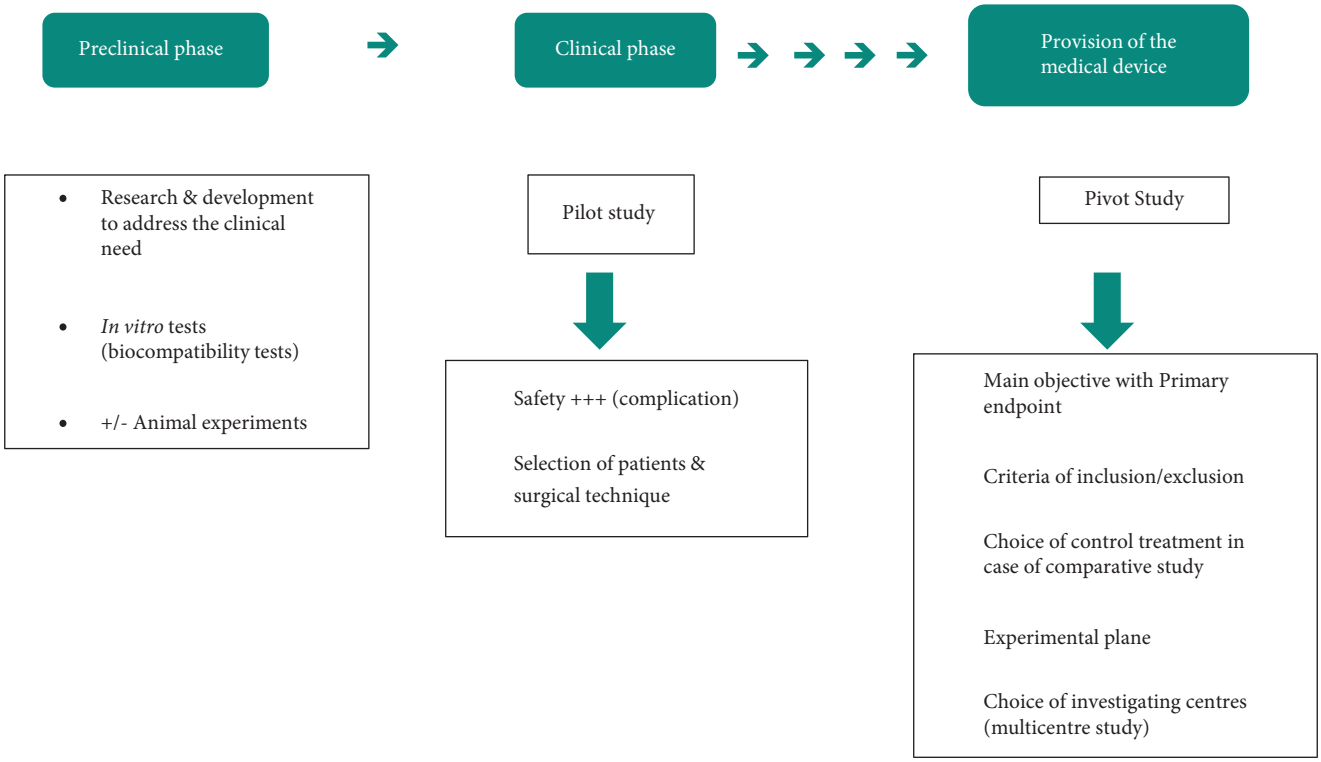
Chung et al. [1] have not mentioned the Versatile Automated Device recently designed by another French team [4], designed to obtain a lower exerted pressure on the urethral tissues and improve continence efficiency according to the patient's activity. In fact, this device includes a sensor, which automatically detects circumstances involving high bladder pressure and adapts the occlusive pressure accordingly. The device was evaluated using isolated goat urethra and, then, *in vivo* with encouraging preliminary results. Research studies (bench and animal) are still running and awaited.

An electromechanical device has also been developed by Valerio et al. [5] and recently tested in animals. Its principle is an electromechanical induction of alternating compression of successive segments of the urethra by a series of cuffs activated by artificial muscles. This ovine study showed that this device could provide continence. This new electronic-controlled sequential alternating compression mechanism avoided damage to urethral

**Table 1** Innovative characteristics of AUS compared with the current AMS 800®.

| Device | More compact than the AMS 800® | Improved control of pressure during stress | Improved detection of the administered pressure | Adjustable | Key remaining questions |
|---|---|---|---|---|---|
| FlowSecure™ | No | Yes | No | Yes | Pump perforation at pressurisation |
| Periurethral Constrictor | Yes | No | Yes | Yes | Controversial results on continence |
| Tape Mechanical Occlusive Device | Yes | No | No | No but simplicity of use with its on/off button | ? |
| ZSI 375 | Yes | No | No | Yes | No multicentre prospective controlled study |
| Versatile Automated Device | Yes | Yes | Yes | Yes | ? |
| Electromechanical Device | ? | Yes | Yes | No | ? |

**Fig. 1** Key steps for the clinical development of a medical device.




vascularity for at least 3 months after implantation. After this positive early step, long-term studies are needed before clinical application can be considered. Table 1 shows the innovative principles of each former model of the AUS.

In conclusion, in an era where AUS use is increasing, a new and more sophisticated device is probably needed. Whatever the use, in men or women, the AUS aims to mimic continence/voiding phases as close as possible to normal conditions. Nobody knows what the future holds for hydraulic and mechanical devices. The above-mentioned devices suggest that further studies are required to assess the safety and efficacy of these new generation AUS devices, in comparison with the so-called 'gold standard' AMS 800®. The developmental steps for these devices must include bench and animal studies, as well as feasibility studies in humans to control for safety and surgical efficiency. Figure 1 provides the main steps of development of medical devices. After a feasibility study to check the proof of concept, any clinical use must be preceded by multicentre controlled studies. All of these studies have to be done under ethical committee approval. The recent USA Food and Drug Administration (FDA) warning (http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/UroGynSurgicalMesh/ucm262299.htm) about prolapse

meshes in women should warn all clinical research teams about the absolute need for careful evaluation for all new implantable human devices.

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