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VIDEO URODYNAMICS IN RATS REVEALS ACTIVE BLADDER DOME FILLING BY DIRECTIONAL CONTRACTION OF THE BASE

Hypothesis / aims of study
Low amplitude, nonvoiding bladder contraction pressure waves are commonly observed during filling in many laboratory animal species during cystometric investigation. Various hypotheses have related these pressure waves to sensory function and they are often used as a surrogate/model for human urgency. Using an in vivo video urodynamics preparation in the rat, the origin of these pressure waves has been determined.

Study design, materials and methods
The urinary tracts of 8 urethane anesthetized rats were exposed via a midline abdominal incision. The distal colons were gently evacuated manually and a loose ligature was placed at the splenic flexure to eliminate fecal migration. The right ureter was cannulated with a PE10 catheter connected to a fluid filled syringe. The left ureter was tied. The pubourethral ligament was cut with microscissors during pubic symphysis removal by ronguers, and the exposed urethral surface was gently cleared for easy visualization.
The edges of the abdominal cavity were suspended from a rack and the abdomen was filled with mineral oil. The bladder was suspended by 8-0 suture tied to the free end of the urachus in order to maintain dorsal-ventral orientation and allow free rostral-caudal movement with filling and emptying. A static, saline-filled PE50 catheter attached to a pressure transducer was inserted into the bladder transurethrally. A video camera was positioned above the LUT to record LUT movements during urodynamics. Video images were taken via a frame grabber using LabView program developed in this laboratory at a rate of 1 per second. Normal saline or saline with trypan blue was infused into the ureter at a physiological filling rate of 0.02-0.04 ml/min. Intravesical pressures were continuously recorded using PowerLab Chart. Images were synchronized to the Chart bladder pressure recordings manually by systematically recording image numbers from the frame grabber to Chart comments.
Analyses of images for dimensional measurements were made using IMageJ. Images from the same series were also conjoined to form time-lapse movies using Windows Movie Maker.

Results
The following sequence of events for normal bladder filling is reported. In all cases, following peristaltic delivery of fluid from the ureter into the bladder base, the bladder base contracted and propelled its contents toward the apex of the bladder dome in a peristaltic-like event, resulting in a simultaneous low amplitude, single-peaked nonvoiding bladder pressure wave. This was repeated throughout the filling phase, and the functional compartmentalization of the bladder into base and dome was readily visible by surface indentations creating a "waist" just caudal to the equator, giving the appearance of a dynamic "peanut" shape. The visual impression of the time-lapse movies during filling was that of a relatively dimension-restricted bellows (the base) inflating a relatively dimension-unrestricted balloon (the dome), until bladder capacity was attained and voiding ensued.
In some animals, following dome expansion by the base contraction, the dome responded with a second contraction. This activity resulted in a double-peaked pre-micturition nonvoiding pressure wave, the first component being derived from the contraction originating in the base and the second from the dome contraction.
At voiding threshold, the distinction between base and detrusor seemed to blur as the bladder contracted down from the apex toward the urethra. During micturition, a statistically significant widening (~60%) of the bladder neck and shortening of the proximal urethra (~20%) was observed.

Interpretation of results
Urine storage by the bladder is a two-stage active process which represents the functional compartmentalization of the bladder rather than a passive filling of the bladder from the bottom up. Whether this process is myogenic or neurogenic in origin is currently under investigation.
The secondary dome contractile response to the filling contraction of the base in some animals may be more in line with what may be considered urgency-related bladder overactivity. These contractions, which produced similar peak pressure amplitudes to those of the bladder base, may be hyperreflexic responses to stretch by the dome. Whether this process is myogenic or neurogenic in origin is also currently under investigation.
As is also reported for the human during video urodynamics, the bladder neck funnels and the proximal urethra shortens during micturition.
Thus, this new methodology has enabled the recognition of a heretofore unrecognized, normal active filling process by rhythmic directional contraction of the bladder base and a step-wise inflation of the bladder dome. Moreover, that these contractions may elicit a dome contraction in response to step-wise stretching in some preparations suggests that these secondary contractions may provide a more reliable model for urgency-related pre-micturition nonvoiding contractions. Conditions which can reliably elicit such contractions are currently under investigation.

Concluding message
Contrary to expectation, bladder filling appears to be an active, rather than a passive process. It may be that the reasons for this phenomenon to go previously unreported include the use of non-physiological filling rates, which may overwhelm the ability of the bladder base and dome to coordinate filling function, or the use of non-physiological filling routes (i.e. non-ureteric filling).
Given the current finding, pathologies or pharmacological treatments which interfere with the active filling process may result in disturbances of storage, such as a lower bladder capacity and/or fluid mechanical conditions favouring stress incontinence.

Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Duke and Durham Veterans Affairs Medical Centers IACUC**