

## **EFFECT OF AGEING ON MODULAR AUTONOMOUS ACTIVITY IN THE ISOLATED MOUSE BLADDER**

### **Aims of Study**

The isolated whole bladder shows complex autonomous contractile activity [1], consistent with a hypothetical modular arrangement of the detrusor muscle [2]. Following a period of partial bladder outlet obstruction in the rat, a recognised model of detrusor overactivity, autonomous activity becomes enhanced and more co-ordinated, resulting in obvious fluctuations in intravesical pressure [3]. The current study examined the integrated activity of the bladder wall in the isolated whole mouse bladder to ascertain whether altered modular activity could be an aetiological factor in detrusor dysfunction associated with ageing.

### **Methods**

Two groups of nulliparous female C57bl mice were studied, 'young' (aged 34 months, n=10) and 'ageing' (14-18 months, n=13). The urinary bladder and urethra were microsurgically removed *post mortem*. A polythene cannula was secured at the bladder neck, and connected to a pressure transducer and a syringe to allow variation of intravesical volume. The bladder was placed in a modified organ bath containing Tyrode's saline bubbled with 95% oxygen, 5% carbon dioxide (30 ml, 36°C, pH 7.4). Intravesical pressure was recorded with Newcastle Photometric Systems hardware and software. Movements in the bladder wall were monitored with a video camera and analysed with proprietary software. Observations were made following equilibration, gentle bladder distension, and in the presence of tetrodotoxin (TTX) and the muscarinic agonist, arecaidine. Appropriate volumes of concentrated drug solutions were placed directly into the organ bath to achieve the required final dilution.

### **Results**

Autonomous activity, comprising localised contractions and propagating waves, was seen in all control mice. In striking contrast, none of the ageing mice showed spontaneous localised or propagating contractions. A substantial difference was also apparent on application of arecaidine, a muscarinic-agonist. In controls this elicited a considerable degree of highly complex activity in the bladder wall. Associated with this were compound pressure effects, with a shift in baseline due to direct muscle response, on which were superimposed pressure fluctuations due to indirect muscle contraction evoked by non-myogenic stimulation. Ageing mice showed the baseline pressure shift with arecaidine, but no pressure fluctuations and none of the complex contractions. Thus, ageing is associated with loss of autonomous activity, while detrusor muscle contractility is preserved. TTX did not influence autonomous activity or the arecaidine responses.

### **Conclusions**

Ageing is associated with a substantial increase in the prevalence of lower urinary tract problems, including irritative and obstructive symptoms, detrusor overactivity and hypocontractility. The current study establishes that ageing is associated with reduced modular autonomous activity in the isolated bladder, with loss of phasic pressure fluctuations and modular contractile activity evoked by muscarinic stimulation in young mice, while the direct muscle response is preserved. Although the relationship between these observations and the recognised clinical sequelae of ageing is unclear, they provide a possible basis for aspects of age-related bladder dysfunction, including detrusor failure and increased post void residual volumes.

## **References**

- 1 Drake MJ, Harvey IJ, Gillespie JI. Autonomous activity in the isolated guinea pig bladder. *Experimental Physiology* 2003; 88: 19-30
- 2 Drake MJ, Mills IW, Gillespie JI. Model of peripheral autonomous modules and a myovesical plexus in normal and overactive bladder function. *Lancet* 2001; 358: 401-3
- 3 Drake MJ, Hedlund P, Harvey U, Pandita RJ, Andersson K-E, Gillespie JI. Partial outlet obstruction enhances modular autonomous activity in the isolated rat bladder. *Journal of Urology* 2003; In press