The contractile and histological properties of human detrusor from children with normal and pathological bladders.

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**Introduction.** Major congenital urinary tract anomalies have life-long functional consequences and require long-term urology follow-up. However, the physiological basis of altered bladder function is unknown. This study aims to demonstrate the detrusor physiology of these conditions. We hypothesised that major congenital anomalies result in measurable differences in detrusor physiology. Direct comparison has been made between normal (control) tissue and that from exstrophy, cloacal exstrophy, cloacal anomalies, neuropathic bladders and posterior urethral valves.

**Methods.** Bladder wall biopsies were obtained from children undergoing repair for congenital anomalies. Detrusor strips, with mucosa removed, were superfused, tied to an isometric force transducer and electrically stimulated to elicit nerve-mediated contractions or exposed to carbachol to elicit contractions. Samples were also stored in formaldehyde, paraffin-embedded, sectioned (5 μm) and stained with Elastin-van Gieson or Masson's Trichrome to assay relative muscle and connective tissue quantities. Data are median [25.75% interquartiles]; sets were compared with non-parametric ANOVA; null hypothesis was rejected when *p<0.05.

**Results**

**Nerve-mediated contractions**

Fig 1: control force-frequency curve for tissue from a control bladder. The estimated maximum tension, $T_{max}$, and f1/2, the frequency for $T_{max}/2$, are shown.

Fig 2 plots $T_{max}$ values for the different groups from whom tissue was sampled. $T_{max}$ was significantly reduced in all groups except cloacal anomalies. f1/2 values were similar in all groups.

**Atropine resistance**

Fig 3: atropine resistance was present in all groups. It was quantified by recording tension at 16 Hz stimulation before and after 1 μM atropine.

**Carbachol contractions**

Fig 4 shows that carbachol (10 μM) contraction strength followed a similar pattern to $T_{max}$ values. EC50 values ([carbachol] for half-maximum effect) were similar in all groups (ε=1 μM).

**Histological assessment**

Fig 5: samples were stained with elastin van Geissen or Masson’s Trichrome to estimate the relative amounts of smooth muscle and connective tissue.

Fig 6 shows the relationship between the smooth muscle/connective tissue ratio and unit contractile strength, $T_{carb}$. There is a significant relationship between the relative smooth muscle quantity and contraction strength $T_{carb}$.

**Discussion and Conclusions.** Bladder wall samples were obtained from neonates and children with a large number of congenital bladder conditions and their in vitro contractile properties compared to those from a control group (children undergoing an open bladder procedure such as ureteric reimplantation, urachal cyst excision or localised bladder tumour excision, with normal bladder function). With nearly all pathological groups contractile function was diminished (with the exception of children with cloacal exstrophy) whether contraction was elicited by the muscarinic receptor agonist carbachol, or stimulation of embedded motor nerves by electrical field stimulation. An unusual feature of the EFS responses was a high proportion of atropine resistance, absent in stable adult human bladders. The relative proportion of smooth muscle and connective tissue was also measured in the biopsy samples. The amount of connective tissue was increased significantly in all pathology groups, except the cloacal anomaly group. The increase of connective tissue was significantly associated with the decline of contractile function.

We conclude that the decline of contractile function in bladder samples from children with congenital anomalies is not due to detrusor failure per se, but a replacement of smooth muscle with connective tissue.

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