

# Bladder control a consequence of maturation: evidence after renal transplantation

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This report contains case studies on three children with early end-stage renal failure due to renal malformation or nephrotic syndrome, but without bladder involvement. All patients became anuric in the second year of life, before having obtained bladder control. They underwent successful cadaveric renal transplantation, having been anuric for almost 2 to 4 years. When the bladder catheter was removed 5 days after transplantation, all three children asked for the urine potty without ever having been prompted. Three weeks after transplantation, all three children achieved complete bladder control during the day, and two of them also at night. These observations add further evidence to the notion that the development of bladder control is a consequence of maturation and not of training.

We have recently demonstrated that development of bladder and bowel control in healthy children is largely a maturational process which cannot be accelerated by an early onset or high intensity of training (Largo et al. 1996). To add further evidence to this concept of maturation, we report on three young children with early chronic renal failure and long-standing anuria. Despite the absence of toilet-training and perception of bladder filling during the sensitive period of emergence for dryness (Mac Keith et al. 1973), all three children reached bladder control within 3 weeks of successful renal transplantation.

## Case reports

### SUBJECT 1

At 5 months of age, this girl presented with pyelonephritis and marked proteinuria which prompted further evaluation. Clinical examination showed a complete situs inversus. Extensive investigations, including renal and liver biopsy and endoscopic retrograde cholangiopancreatography (ERCP), revealed the diagnosis of familial progressive tubulointerstitial nephropathy and primary sclerosing cholangitis (Neuhaus et al. 1997). Renal function and urine output declined, and the girl presented at 1 year 11 months with end-stage renal failure. Peritoneal dialysis was commenced and within a few weeks she became anuric before she had achieved bladder control. Bowel control developed at the age of 3 years. At 5 years 11 months – after an anuric period of almost 4 years – she underwent a successful renal transplantation. Intellectual development, as assessed at the age of 6 years 2 months, was normal for age (IQ 99). Motor development was slightly retarded due to moderate hypotonia.

### SUBJECT 2

At 5 months of age, this boy had presented with bronchitis. Work-up showed a metabolic acidosis, and subsequently chronic renal failure was diagnosed, with a plasma creatinine of 174  $\mu\text{mol/L}$ . Further investigations, including ultrasound and renal and liver biopsy, revealed the diagnosis of renal-hepatic-pancreatic dysplasia (Neuhaus et al. 1996). Renal function deteriorated rapidly, and at the age of 14 months he presented with end-stage renal failure. Peritoneal dialysis was commenced and – as with subject 1 – he became anuric

within a few weeks without having achieved bladder control. Bowel control developed at the age of 2 years 6 months. At 3 years 8 months – after an anuric period of more than 2 years – a successful combined liver–kidney transplantation was performed. Intellectual performance at the age of 6 years was in the low normal range (IQ 88). Motor development was delayed by marked hypotonia.

#### SUBJECT 3

At 3 months of age, this girl presented with an abdominal mass. Subsequent investigations revealed the complete triad of Denys–Drash syndrome (Coppes et al. 1993): Wilms' tumour of the right kidney, nephropathy due to diffuse mesangial sclerosis and male pseudohermaphroditism (female phenotype, 46XY male karyotype). A missense mutation in exon 9 of the Wilms' tumour suppressor gene *WT1* was found. The right kidney was removed and the girl underwent chemotherapy for 4 months. She became progressively nephrotic and her renal function and urine output declined. At the age of 1 year 8 months she was in end-stage renal failure without having achieved bladder control. Peritoneal dialysis was commenced and simultaneously the left kidney was removed. Bowel control developed at the age of 3 years. At 4 years 2 months – after an anuric period of 2 years 6 months – she underwent a successful renal transplantation. Intellectual development, as assessed at the age of 2 years 1 month, was normal for age (IQ 89). Motor development was slightly retarded due to moderate hypotonia.

#### Development of bladder control after renal transplantation

Five days after renal transplantation, the bladder catheter was removed in all patients. Subsequently all three children spontaneously asked for the urine potty. They took the initiative without having been prompted either by nurses or parents. Three weeks after renal transplantation, all three children had achieved complete bladder control during the day. Two of them (subjects 1 and 2) were also completely dry at night whereas one girl (subject 3) was intermittently bed-wetting. So far – after 4 years, 1 year, and 2 months respectively – all three subjects have remained dry.

#### Discussion

In the Zürich longitudinal study, a major change in toilet-training was observed in two successive generations of healthy children. Although the median onset of toilet-training was delayed by 13 months in the younger generation, bladder control by day and at night was not affected (Largo et al. 1996). This observation was consistent with previous reports indicating that maturation rather than toilet-training was the major determinant of bladder control (Klackenberg 1971, Largo and Stutzle 1977). The rapid development of bladder control after renal transplantation in three children with long-standing anuria – none had yet obtained bladder control before becoming anuric – adds further evidence to this concept. In these three children, bladder control developed without toilet-training; neither parents nor nurses initiated this process. Perception of bladder filling and urge to urinate were present within a few days, and dryness emerged despite the apparent omission of the sensitive period between 1 and 4 years of age (Mac Keith et al. 1973).

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