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Obstructive Uropathy in Infants

Obstructive uropathy in infants is a complex disease. It is a major cause of renal failure in early life, yet many aspects are poorly understood. Improvement in renal function after surgical relief of the obstruction is variable and unpredictable: the frequent association of renal dysplasia (Bernstein 1968) and pyelonephritis contributes to unsatisfactory surgical results. It is clear that persistent obstruction to the flow of urine may result in progressive destruction of renal tissue (Hodson 1967): in experimental hydronephrosis there is a correlation between the duration of obstruction and the final improvement in renal function after relief of obstruction (Kerr 1956). It might seem, then, that infants with urinary tract obstruction, in whom the anatomical lesion is frequently congenital, would rarely improve after surgery. Nevertheless, we have observed significant improvement in GFR in some infants after operation (Table 1), but have not found it possible on clinical or radiological grounds to predict the potential for recovery of renal function.

In some circumstances, it may be difficult to decide whether significant obstruction is present. In situations where the whole urinary system is malformed, as, for instance, with agenesis of the abdominal muscles (Williams 1968), the classical radiological deduction that dilatation of the urinary tract implies obstruction is not always valid. Doubt about the presence of obstruction may also arise where dilatation persists after apparently satisfactory relief of obstruction, and the surgeon may have to decide upon operative intervention on insecure grounds. An assessment of the probable benefit of surgery to renal function would materially assist the surgeon in such cases.

There is thus need for another approach to the diagnosis and assessment of urinary tract obstruction. Although direct measurement of the intrapelvic pressure seems rational (Struthers 1969) there are technical problems: direct pelvic puncture or nephrostomy is necessary, and pressure measurements must be recorded during maximum diuresis for meaningful pressure-flow relationships to be obtained. Isotope renography is feasible, though technically difficult in young children (Wenzl *et al.* 1965), but is a field that has not been adequately explored. We are, however, examining the possibility that there are functional characteristics of the obstructed kidney which could be used to support the diagnosis of significant obstruction, in the hope of establishing a simple clinical test applicable to sick infants which would enable the surgeon to predict the benefit in renal function to be obtained from relief of a presumed obstruction.

Water Excretion in Obstructive Uropathy

The inability of the obstructed kidney to concentrate the urine is well established (Berlyne 1961), but the large residual volume of urine makes this parameter difficult to evaluate. A more accessible function is the capacity of the obstructed kidney to dilute the urine. Kiil & Auckland (1961) showed that increased ureteric pressure in one kidney of a dog during water diuresis resulted in a diminished flow rate and sodium concentration with increased osmolality and creatinine concentration in the urine of the affected kidney relative to that of the control kidney. The findings point to increased water reabsorption in the proximal tubule, distal tubule or both; the diminished sodium concentration supports a predominantly proximal effect. These results in acute obstructive uropathy were confirmed by Suki *et al.* (1966) who pointed out the similarity of the functional disturbances to those of renal artery stenosis: in both, the fractional excretion of filtered water, V/GFR (V=urine flow rate), during water diuresis was lower on the affected side. In contrast, these authors showed that the chronically obstructed kidney under similar conditions excreted a larger fraction of filtered water than the control kidney; here V/GFR was higher on the affected side.

This increase in fractional proximal reabsorption in acute obstructive uropathy accounts for the characteristic nephrogram seen during intravenous pyelography, for the density of the nephrogram is determined by the total dose of contrast medium and the extent of proximal tubular reabsorption of water (Saxton 1969).

The distinction between renal function in the acute and chronic obstruction experiments of Suki *et al.* (1966) may not be temporal; in their experiments ureteric pressure was higher in the acute group than in the chronic. It may be that intrapelvic pressure rather than duration of obstruction is the determinant of the functional differences observed: in the rat at least, only relatively high ureteric pressures are transmitted back to the proximal tubule (Gottschalk & Mylle 1956). But, in spite of these provisos, and the uncertainty of extrapolation from animal experiments to the heterogeneous situation of human disease, these observations provide potential guidelines for clinical study. Whatever the physiological interpretations of the observations, it may be that those kidneys which behave as the

Table 1
Patients arranged in order of improvement in GFR at one week

Patient	Age	Diagnosis		GFR (ml/min/1·73 m² surface area)			Maximum $P_c/U_c \times 100$	△ GFR%
		Left	Right	Pre-operative	Post-operative 1 week	Post-operative 3 months	pre-operative	at one week
AP	11 months	UV	UV	102	207	168	8·1	+ 102
SS	5½ years	UV	UV	91	130	—	8·2	+ 42
MH	2 months	PUJ	PUJ	69	91	—	6·3	+ 32
PD	4½ years	UV	UV	40	53	51	17·4	+ 27
AM	4 months	?UV	NonF	44	54	57	25·7	+ 24
ME	10 years	Urethral valves		115	135	—	10·8	+ 17
BP	5 months	?UV	?UV	50	58	45	11·5	+ 16
JF●	5 months	NonF	PUJ	56	58	—	3·4	+ 4
DW	7½ years	UV	UV	66	68	68	11·3	+ 2
KZ	5½ years	?PUJ	NonF	120	106	88	13·4	— 11

UV, ureterovesical junction obstruction. PUJ, pelvi-ureteric junction obstruction. NonF, non-functioning kidney
Maximum $P_c/U_c \times 100$ during water diuresis in 5 healthy adults was 10·1 ± 0·5 (S.D.)
●Water-loading in JF was unsatisfactory (*see* text)

acutely obstructed model, that is, excrete a smaller fraction of filtered water during water diuresis, would show the greatest improvement in function when the obstruction is relieved. We are therefore examining the hypothesis that the increase in GFR after surgery can be predicted from the fractional excretion of filtered water during pre-operative water diuresis.

Methods

Investigation of renal function in infants with obstructive uropathy poses many technical problems: sick infants do not tolerate investigative procedures well and classical clearance techniques are not applicable. Repeated venepunctures are unacceptable: analytical techniques must be scaled down for capillary blood sampling. The large residual volume of urine in obstructive uropathy precludes accurate timed urine collection. Passage of catheters above the site of obstruction does not overcome the problem, for the kidneys will no longer be obstructed. Furthermore, if any function of the kidney is acutely stressed, the large residual volume may mask the renal response; it is important to demonstrate that the relevant urinary parameter has reached a plateau before it can be concluded that the urine passed externally is representative of that excreted by the kidney and that the full range of renal function has been observed.

GFR was calculated from the plasma clearance of ^{51}Cr-ethylene-diamine-tetra-acetic acid (^{51}Cr-EDTA) (Chantler *et al.* 1969). This technique is especially suited to the study of obstructive uropathy since urine collections are not required; using an intravenous dose of 1 μCi/kg it was possible to obtain satisfactory exponential decay curves with capillary sampling. GFR was estimated during a water diuresis which was initiated with 1,400 ml H_2O/1·73 m² surface area by mouth or nasogastric tube in infants who were already well hydrated and maintained for at least 5 hours by the replacement of urine losses with an equal volume of water.

Fractional excretion of filtered water (V/GFR) was estimated from urine and plasma creatinine concentrations (U_c and P_c). If creatinine clearance is taken as an estimate of GFR, the following relationships hold:

$$\frac{V}{GFR} = \frac{V}{U_c V/P_c} = \frac{P_c}{U_c}$$

and the V term, which is unmeasurable, has been eliminated. True plasma creatinine was measured after absorption on to an ion-exchange resin (Stoten 1968): this tedious procedure is essential in infants because true plasma creatinine levels are lower and the artifact of non-creatinine chromogens relatively greater than in adults (Doolan *et al.* 1962).

Results

GFR and fractional excretion of filtered water during water diuresis were measured pre-operatively in 10 children with obstructive uropathy. These were children in whom independent surgical opinion considered that relief of urinary tract obstruction was necessary. In all cases a plateau of V/GFR (P_c/U_c) was demonstrated. GFR was again estimated one week after operation during water diuresis.

The clinical details and results are shown in Table 1. The cases have been arranged in order of increase in GFR, calculated as:

$$\triangle GFR\% = \frac{GFR\ post\text{-}op. - GFR\ pre\text{-}op.}{GFR\ pre\text{-}op.} \times 100$$

P_c/U_c was measured during water diuresis in 5 normal adults and the range obtained was surprisingly small: 10·1% ± 0·5% (S.D.). The three children who had the greatest increase in GFR one week after relief of obstruction excreted a small fraction of filtered water, i.e. lower values of P_c/U_c than the adult controls; the other 6, who had less improvement of GFR, gave values of P_c/U_c greater than the adult mean value. One

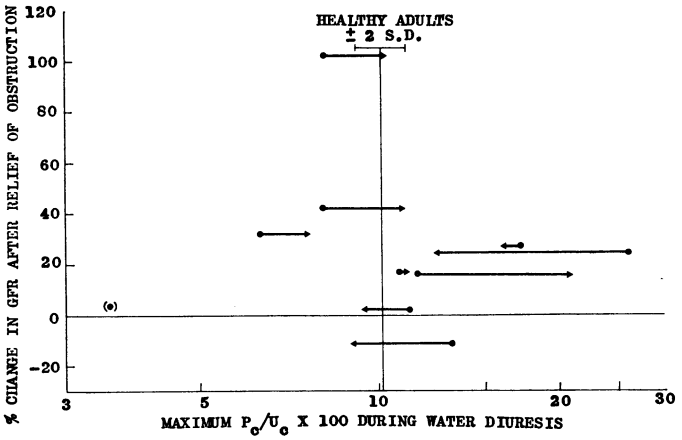

Fig 1 *The relationship between* $\triangle GFR\%$ *at one week and maximum* $P_c/U_c \times 100$ *during water diuresis.*
● = *pre-operative.*
◀ *and* ▶ = *post-operative*

child (J F) has been excluded from this analysis because the water-loading experiment was technically unsatisfactory and his urine remained hypertonic to plasma during the test: this difficulty was due to an exceptionally large residual volume in a pelvi-ureteric obstruction.

The relationship between $\triangle$ GFR% and pre-operative P_c/U_c during water diuresis is shown in Fig 1. P_c/U_c was also measured during water diuresis post-operatively: it is noteworthy that this parameter returned towards the adult normal range in the 3 patients who had the lowest value for P_c/U_c and the larger increments in GFR. Two of these 3 patients had acquired ureterovesical junction obstruction; the third had congenital bilateral pelvi-ureteric junction obstruction.

The data conform with the distribution predicted from the experimental work and provide suggestive evidence that the benefit to renal function can be forecast from the response to a pre-operative water load, but more cases need to be studied. We are also estimating the GFR 3 months after operation, by which time the maximum improvement is likely to be achieved (Kerr 1956). Data obtained to date are included in Table 1 and support the tentative conclusions based on the data at one week after operation.

It is likely, however, that the best assessment of the role of surgery in obstructive uropathy will entail a combination of clinically radiological, functional, renographic and manometric data.

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Meeting November 27 1969

The following cases were presented:

Advanced Carcinoma of the Kidney Treated by Hormones
Professor A C Thackray

Tumour in Renal Cyst (Two Cases)
Dr R C B Pugh

Bladder Cancer Presenting as Interstitial Cystitis (Three Cases)
Dr N J Brown

Alleged Small Hæmangiomas Causing Bleeding from the Lower Urinary Tract (Three Cases)
Dr C K Anderson