

Pyelonephritis.
XIII. Effect of Congenital Hydronephrosis on Treatment
of Experimental Pyelonephritis¹ (36453)

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Previous studies in this laboratory of experimental *Streptococcus faecalis* pyelonephritis in rats with unilateral hydronephrosis due to partial right ureteral obstruction have demonstrated that hydronephrosis both predisposed the affected kidney to acquisition of *S. faecalis* infection (1) and allowed a significant increase in the renal microbial population as compared to nonhydronephrotic kidneys (2). This report extends our observations to the effect of unilateral hydronephrosis upon response to antibiotic treatment.

Methods and Materials. The methods of the experimental infection have been published in detail previously (1-3). Briefly 100-200 g male Slonaker-Addis rats² were separated into hydronephrotic (right kidney) and nonhydronephrotic groups by intravenous pyelography with 1 ml of 50% sodium diatrizoate. Rats were inoculated intravenously with 1 ml of an 18 hr brain-heart infusion broth culture of *S. faecalis* ATCC 23241 containing $1.2-2.3 \times 10^9$ organisms/ml. Two weeks after inoculation treatment was begun with 25,000 units procaine penicillin G intramuscularly twice daily in approximately one-half the rats. Treatment was continued for 21 days, and the animals were sacrificed 7 days later. At the time of sacrifice the midportion of each kidney was fixed in 10% buffered formalin; the balance was homogenized and quantitatively cultured. Bacterial content was expressed as log number *S.*

faecalis per gram of kidney tissue. A kidney was considered infected if any bacteria were found. The assay method allowed recovery of as few as 10 microorganisms/g tissue.

Results. Penicillin treatment in rats with two radiographically normal kidneys was effective in significantly reducing both the mean renal microbial population and the proportion of kidneys infected at the time of sacrifice (Table I). In rats with unilateral hydronephrosis treatment did not have a statistically significant effect in either the hydronephrotic right or the radiologically normal left kidneys (A vs C and B vs D, Table II). Nevertheless, in treated animals with unilateral hydronephrosis the hydronephrotic right kidneys had a significantly higher renal microbial population than their paired normal (left) kidneys (C vs D, Table II).

Sections from the midportion of each kidney were examined microscopically for evidence of acute or healing inflammation. Changes in both hydronephrotic and normal kidneys were similar to those described previously (2) but more extensive. When evaluated for number and size of involved areas using the previous criteria and scoring on a 0-3+ scale, no significant differences could be seen among the groups.

Discussion. Extensive clinical experience has led to the widely held belief that even partial ureteral obstruction not only predisposes to pyelonephritis but also results in an infection which is harder to treat (4). Little experimental evidence has been available to confirm this impression, as previous work relates primarily to experimental infection in the kidney with sudden complete or partial

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² Breeding stock obtained from A. L. Sellars, Cedars-Sinai Medical Center, Los Angeles, CA.

TABLE I. Effect of Penicillin Treatment^a on Experimental *S. faecalis* Pyelonephritis in Slonaker-Addis Rats with Radiologically Normal Kidneys.

Group	No. of kidneys	No. infected	Log/g kidney tissue
Not treated	62	56 ^b	4.92 ± 0.270 ^c
Treated	58	37 ^b	3.25 ± 0.365 ^c

^a 25,000 units procaine penicillin G intramuscularly twice a day.

^b Chi-square = 10.62, $p < .005$.

^c $t = 3.70$, $p < .001$.

ureteral obstruction (5), which may not be comparable to the usual situation in the patient.

In an earlier study designed to explore whether the hydronephrotic kidney was more susceptible to infection, an inoculum size was chosen (10^6 per ml) which would infect only half the normal kidneys. In this situation the increased susceptibility of the hydronephrotic kidney was easily demonstrable (1). For the present experiments in order to have as many kidneys as possible infected before the start of treatment, an inoculum of 10^9 per ml was used. Over 90% of normal untreated kidneys were infected at the time of sacrifice (Table I).

For comparative study of the effect of treatment on normal and hydronephrotic kidneys the penicillin dose (50,000 units/day) was chosen to reduce the renal microbial population of the normal animals without elimi-

nating infection from the majority. This allowed evaluation of antibiotic effects due to the presence of unilateral hydronephrosis, which might otherwise be obscured by larger doses of penicillin.

The use of a high inoculum combined with the 2 week delay before treatment began and the relatively low dose of penicillin probably account for the failure to find significant pathological differences among the various groups of kidneys.

When this inoculum and treatment regimen were employed, clear differences in the effect of treatment were seen, showing that the hydronephrotic kidney was, indeed, more difficult to treat successfully (A vs C, Table II) and suggesting that in the presence of one hydronephrotic kidney even a contralateral normal kidney may be less responsive to treatment (B vs D, Table II).

Summary. To determine the effect of hydronephrosis on treatment of pyelonephritis, 85 Slonaker-Addis rats with congenital right unilateral partial ureteral obstruction and 120 with two normal kidneys were infected intravenously with *Streptococcus faecalis*. Two weeks after infection one-half of each group was treated with 25,000 units penicillin G twice daily for 3 weeks. Measurement of renal microbial population after therapy ended indicated that the efficacy of treatment was significantly impaired not only in the hydronephrotic (right) kidney, but also in the contralateral normal (left) kidney.

TABLE II. Effect of Penicillin Treatment^a on Experimental *S. faecalis* Pyelonephritis in Hydronephrotic and Normal Kidneys of Rats with Unilateral Hydronephrosis.

Group	Treatment	No. of kidneys	No. infected ^b	Log/g kidney tissue ^c
Hydronephrotic (right) kidney	No	41	34	(A) 4.54 ± 0.372
Normal (left) kidney		41	35	(B) 4.12 ± 0.340
Hydronephrotic (right) kidney	Yes	44	36	(C) 4.52 ± 0.403
Normal (left) kidney		44	32	(D) 3.42 ± 0.368

^a 25,000 units procaine penicillin G twice a day.

^b Statistical comparisons by chi-square: A vs B, C vs D, A vs C, and B vs D all not significant.

^c Statistical comparisons by Student's t test: A vs B, $p < .4$; C vs D, $p < .05$; A vs C, $p < .7$; B vs D, $.1 > p > .05$.

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