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This Week's Citation Classic

Wrong O & Davies H E F. The excretion of acid in renal disease.
Quart. J. Med. **28:**259-313, 1959.
[Univ. Dept. Med., Manchester Royal Infirmary and Medical Unit, Cardiff Royal Infirmary, UK]

The paper describes the urinary response to an acid load, taken as a single oral dose of ammonium chloride. Study of normal subjects and patients with different forms of kidney disease distinguished the factors influencing urinary acidification and ammonium excretion. [The *SCI*® indicates that this paper has been cited over 475 times since 1961.]

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"This work was conceived in 1954 at the Manchester Medical School, where I was a junior teacher in the department of medicine of Robert Platt, then the doyen of British renal physicians. I was single, with military service, medical residencies, and exams behind me, and had just returned from Boston anxious to put the lessons learnt from Fuller Albright and Alex Leaf into effect. The University provided a pittance of £640 a year as salary, lodging in the nearby student residence, laboratory facilities, and modest clinical and teaching responsibilities. The seniors in the department, Douglas Black and Bill Stanbury, were liberal with ideas and expertise, but did not try to enroll me in their research, so I teamed up with Howard Davies, then a Medical Research Council research fellow, to study renal tubular function in hyperparathyroidism —a topic combining two of the main departmental interests.

"We naively proposed to study *all* tubular functions, concentrating on the distal tubule as being more important clinically. Water conservation had been fairly well worked out, so we turned to acid excretion, meaning to later tackle the more difficult problems of sodium and potassium conservation. It was easy to establish an acid load test which was completed in a working day (and so did not require hospital admission). In fact, we never changed our initial protocol as this test caused excretion of a maximally acid urine within two hours of the acid load.

"We were fortunate that one of our first patients without parathyroid disease had renal calcification (nephrocalcinosis) and turned out to have a marked defect in urinary acidification without acidosis, which we named 'the incomplete syndrome of renal tubular acidosis.' Inevitably we extended our interests to other forms of renal disease. Manchester colleagues referred us many patients of interest, and Charles Dent in London generously collected patients whom I drove down to study on Sundays, spending the small hours of the morning running urine analyses and getting to know the hospital where I now work. Within four years, 68 subjects had been studied and we had a mammoth manuscript which Robert Platt thought too indigestible to stand much chance of publication, though he was kind (or prescient) enough to remark, 'Of course, it will be a classic.'

"I suspect the paper has been quoted mainly by those following our test procedure, though some of our other findings were of greater theoretic interest, particularly the low urinary PCO_2 in tubular disease and the direct relationship of stimulated ammonium excretion to glomerular filtration rate in all forms of renal disease. In retrospect we attached too much importance to potassium depletion as a cause of acidification defect, but the paper's chief omission was our failure to recognise proximal ('Type II') renal tubular acidosis, then undescribed, and so rare that we didn't encounter a case.

"Looking back to my years in Manchester, I realise what an excellent education they provided by giving me time to tackle my own problems under a benign yet critical supervision. Because of earlier marriage, and the rigidity of our postgraduate medical training programme, few of our present graduates feel able to afford such self indulgence."