

# ANURIA FOLLOWING PENICILLIN ADMINISTRATION

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Untoward reactions to penicillin have given rise to increasing concern over recent years. Anuria occurring as a manifestation of penicillin sensitivity has been described on a few occasions. Langdon described exfoliative dermatitis and renal shut-down occurring in a 53-year-old male after an injection of penicillin.<sup>1</sup> Swann and Merrill<sup>2</sup> recorded 5 days of anuria in a 48-year-old male which they ascribed to penicillin sensitivity. Carré and Squire<sup>3</sup> described the case of a girl of 8 months who 1½ hours after an injection of crystalline penicillin for earache, vomited, appeared shocked, and

passed excessive quantities of urine; after a second injection she developed an evanescent erythematous rash and anuria.

In the following case of anuria in infancy it is suggested that the anuria was a sensitivity reaction to penicillin.

## CASE REPORT

A European boy of 13 months was admitted to Groote Schuur Hospital on 3 February 1955 because of failure to pass urine. He had been well until 30 January, when he developed symptoms of an upper-respiratory-tract infection. On 1 February he was given an injection of procaine penicillin by his private practitioner. Soon after the injection he became restless, cried much, and vomited

persistently. He failed to pass urine after the morning of 2 February and at the time of admission had been anuric for 30 hours. He was constipated and had become increasingly drowsy over the 24 hours preceding admission.

He was a well nourished child weighing 22 lb., apyrexial, and showing no clinical evidence of dehydration. The bladder was not palpable and the genitalia were normal. The systolic blood pressure was 99 mm. Hg. The ocular fundi were normal.

*Special Investigations.* Haemoglobin 10.6 g.%. White blood count 7,350 per c.mm. Blood urea 200 mg.%. Serum: Na 124.3 mEq./per l., Cl 88 mEq./per l.  $\text{CO}_2$ -combining power 26 vols.%. Wassermann reaction negative.

#### Course and Treatment

The patient was fed on 5% dextrose solution. During the night he started to vomit and passed dark, liquid stools. The vomiting became more persistent over the course of the next day, despite feeding by gastric drip and an injection of 12½ mg. of Largactil. His condition deteriorated and on the evening of 4 February he developed generalized convulsions. The systolic blood pressure at this stage was 110. The convulsions were controlled by intramuscular injections of 2 ml. of paraldehyde and ½ gr. of sodium gardalen, and lumbar puncture. The cerebrospinal fluid was normal.

On the morning of 5 February the child passed approximately 2 ml. of urine, containing albumin but no other abnormal constituents. On 5 February, when anuria, apart from this, had lasted 84 hours the stomach was washed out, with the return of much mucus and some blood. A modified 'Borst' regime was instituted: a mixture consisting of 40 g. of salt-free butter, 160 g. of glucose and 240 ml. of water per 24 hours was given by stomach tube, and 24-hour urinary collections were started. At the end of the first 24 hours on this regime the mixture had been well retained; anuria was still present, but the patient's general condition had improved and the convulsions had not recurred.

The patient started to pass urine during the second day of the regime (7 February); 55 ml. was passed, after an anuric phase of 96 hours. This urine contained a trace of albumin and scanty hyaline and epithelial casts. 60 ml. of M/6 sodium lactate was added to the gastric drip to compensate for the volume of urine passed and to combat the tendency to acidosis.

The blood chemistry after the first diuresis was as follows: Na 131.8 mEq. per l., Cl 74.0 mEq. per l., K 2.55 mEq. per l.,  $\text{CO}_2$ -combining power 39 vols.%, blood urea 279 mg.%. To correct the low serum Na, Cl and K 1 g. of NaCl and 0.5 g. of KCl were added to the gastric drip. Over the next few days the urinary volume increased progressively. The intake was accordingly increased. When vomiting occurred its volume was assessed and an equal quantity of the 'Borst mixture' was added to the gastric drip. In view of repeatedly low serum Na, K and Cl electrolytes were added to the feeds, as shown in Table I. By 13 February the patient was taking cow's milk from a bottle and a few days later he was on a mixed diet.

On 17 February a generalized urticarial eruption developed, which responded to Benadryl.

The blood-urea level gradually fell until by 23 February it had reached 34 mg.%. The 24-hour urinary volume at this stage was 630 ml. and the specific gravity was 1.012. A subcutaneous pyelogram revealed adequate concentration and excretion of Uriodone.

*Investigation of Sensitivity.* Dilute solutions of penicillin in saline were used for intradermal injections. Areas of redness 1.5 cm. in diameter but without induration developed in response to a solution containing 2.5 units in .01 ml. No redness was obtained in a control. Solutions of procaine hydrochloride did not produce any reaction. Attempts to demonstrate the presence of specific antibodies by the Prausnitz-Küstner technique were unsuccessful.

*Subsequent progress.* One month after discharge the patient developed an attack of gastro-enteritis during which he became dehydrated so as to require a subcutaneous infusion, but the urinary output remained satisfactory.

#### Management

As indicated above, a conservative dietary regime was employed, a high-calorie, high-carbohydrate, protein-free and electrolyte-free diet being given, with restricted fluids.<sup>4,5</sup> The caloric requirement was assessed on the basis of 100 calories per kg. per day. This was supplied by means of a mixture of salt-free butter and glucose in the proportion of 1 to 4 in a volume of water equivalent to the estimated insensible fluid loss. The insensible fluid loss was calculated on the basis of 1 g. per kg. per hour.<sup>6</sup> This estimate may well prove too conservative, especially when diarrhoea occurs. With the onset of diuresis the volume of the fluid intake was increased by an amount equal to the urinary loss. The fluid intake was further increased by amounts approximately equal to the diarrhoeal fluid loss.

Biochemical analysis of the blood was carried out frequently and electrolytes added as indicated by the results, once diuresis had started. Hypokalaemia developed despite protracted anuria. This was probably due to potassium being lost in the diarrhoeal stools and was corrected by the addition of Darrow's solution and KCl. When hyponatraemia occurred additional NaCl was prescribed. M/6 sodium lactate was given when acidosis was marked. When vomiting occurred its volume was assessed and corresponding additional quantities of the 'Borst' mixture were given.

#### DISCUSSION

This case showed several of the features which characterize acute tubular necrosis. Although vomiting was frequent there was never any clinical evidence of dehydration as a cause of the anuria; nevertheless the rapid development of high blood-urea levels suggested that some degree of dehydration was in fact present. Despite an adequate fluid intake after

TABLE I. SHOWING THE MAIN BIOCHEMICAL FINDINGS AND THE TREATMENT

Feb.	Serum					Urine				Intake		
	Na	K mEq./l.	Cl	$\text{CO}_2$ combining power vols.%	Urea mg.%	Na mEq./l.	K mEq./l.	Cl	Vol. ml.	S.G.	Vol. ml.	Composition
3	124	4.4	88	26	200						ad lib	5% dextrose.
5	110	4.1	72	23	205						213	213 ml. 'Borst'.
7	132	2.6	74	39	279	28.8	36.3	38.5	55	1.010	294	234 ml. 'Borst' + 60 ml. M/6 Na lactate.
8	130	3.1	78	40	264	50	31.7	45.9	213	1.040	308	308 ml. 'Borst' + 1 g. Na Cl + 0.5 g. KCl.
9						40.2	24.7	39.3	342		470	350 ml. 'Borst' + 120 ml. Darrow's solution.
10	146	2.5	91.1		214	35.3	21.1		305	1.028	720	480 ml. 'Borst' + 240 ml. ½ strength Darrow's.
11									366	1.018	900	450 ml. milk + 150 ml. Darrow's solution + 300 ml. water.
12									404	1.023	900	690 ml. milk + 210 ml. water + 1 g. KCl.
13									216	1.041	900	Milk.
14					148				221	1.039		Mixed diet.
23					34				630	1.012		Mixed diet.

The serum levels of sodium, chloride and potassium fell during the course of the illness. The volume and electrolyte content of the stools were not estimated; consequently accurate replacements could not be made.

admission there was still no passage of urine. The hypoelectrolytaemia was probably due to loss of electrolytes in the vomitus and in diarrhoeal stools. While the serum levels of sodium and chloride were low, the urine in the early diuretic phase contained considerable quantities of these ions, a finding in keeping with the diagnosis of acute tubular necrosis.<sup>7</sup>

Acute nephritis may cause anuria. In this case there may have been an antecedent throat infection, but the renal shut-down followed too rapidly for acute nephritis unless there had been a pre-existing renal lesion. The subsequent normal renal function argues against pre-existing renal disease.

Conclusive evidence that the anuria was due to penicillin sensitivity is lacking, but the development of vomiting and restlessness soon after the injection is highly suggestive. The positive response to the intradermal injection of a dilute solution of penicillin is an interesting feature. The development of urticaria 16 days after the injection of penicillin may have been a delayed sensitivity reaction. There was no story of previous penicillin administration, but fatal reactions are reported to have followed the first injection. Sensitization may also result from a previous fungus infection. The similarity between this patient and the case described by Carré and Squire<sup>3</sup> is very striking.

It is suggested that vascular spasm resulted from sensitivity to penicillin. This in turn led to renal ischaemia and acute tubular necrosis. Vomiting, with the later development of diarrhoea, may have been contributory factors in the production of this syndrome.

#### SUMMARY

A case of anuria occurring in a 13-month-old boy after an injection of penicillin is described.

A conservative dietary regime was employed, with a high-calorie, high-carbohydrate, protein-free and electrolyte-free diet and restricted fluids.

It is suggested that the anuria was a sensitivity reaction to penicillin.

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#### REFERENCES

1. Langdon, E. (1950): U.S. Armed Forces Med. J., 1, 210.
2. Swann, R. C. and Merrill, J. P. (1953): Medicine, 32, 215.
3. Carré, I. J. and Squire, J. R. (1956): Arch. Dis. Childh., 31, 512.
4. Borst, J. G. G. (1948): Lancet, 1, 824.
5. Bull, G. M., Joekes, A. M. and Lowe, K. G. (1949): *Ibid.*, 2, 229.
6. Levine, S. Z., Kelly, M. and Wilson, J. B. (1930): Amer. J. Dis. Child., 39, 917.
7. Bull, G. M., Joekes, A. M. and Lowe, K. G. (1950): Clin. Sci., 9, 379.