Medical Memoranda

Rapid, Simple Method for Determining Effectiveness of D-Penicillamine Therapy in Cystinuria

Brit. med. J., 1965, 2, 521

Recently this journal carried articles (Crawhall *et al.*, 1963, 1964) describing the effectiveness of D-penicillamine as a therapeutic agent in patients with cystinuria. Similar reports by others have also appeared elsewhere (Lotz and Potts, 1964; Lotz *et al.*, 1965; Bartter *et al.*, 1965).

The rationale involved in the use of D-penicillamine in this disease is simple. Cystine stones form in the urinary tract because of the relative insolubility of cystine, which is excreted in excess. To render cystine more soluble D-penicillamine is given, which converts cystine to a new more soluble compound, penicillamine-cysteine disulphide. Most of the unreacted D-penicillamine is either oxidized to penicillamine disulphide or excreted unchanged.

However, no simple office procedure has been devised to enable the physician to gauge the amount of D-penicillamine required for effective therapy. Reported methods are expensive, elaborate, and time-consuming. We have found recently that the standard nitroprusside cyanide test (Lewis, 1932) and a

simple ferric chloride test are very useful in this regard. Our simple, rapid procedure for following the effectiveness of D-penicillamine is possible because penicillamine-cysteine disulphide and penicillamine disulphide do not give positive tests with nitroprusside cyanide or with 3% FeCl₃, whereas cystine, of course, is positive with nitroprusside cyanide and D-penicillamine is positive with both tests (Table I).

As D-penicillamine is only very rarely excreted unchanged, even with high dosages, it is unlikely to present a source of confusion by giving a positive nitroprusside cyanide test. When in doubt one can exclude the presence of significant amounts of D-penicillamine in the urine by the FeCl₃ test, which is performed by adding 3% FeCl₃ dropwise to the urine. A positive test is indicated by the immediate appearance of a blue colour which fades quickly.

Therefore when the nitroprusside cyanide test becomes negative on an aliquot from a 24-hour urine of adequate but not excessive volume from a patient with cystinuria receiving D-penicillamine one can say with reasonable certainty that the amount of cystine being excreted is less than 100 mg./g. creatinine (Harris and Warren, 1953)—an amount which we feel should not support stone formation.

Spot tests during the day are not recommended, as the variable quantities of cystine, penicillamine disulphide, and penicillamine-cysteine disulphide being excreted in any brief interval will tend to give misleading results.

The results of these simple tests were verified on a Beckman-Spinco automatic amino-acid analyser (Table II). The details are published elsewhere (Lotz *et al.*, 1965).

MYRON LOTZ,* M.D.

JOHN T. POTTS,† M.D.

FREDERICK C. BARTTER,* M.D.

Clinical Endocrinology Branch* and Section on Molecular Diseases,† Laboratory of Metabolism, National Heart Institute, National Institutes of Health, Bethesda 14, Maryland, U.S.A.

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TABLE I.—Test Reactions

	Nitroprusside Cyanide	FeCl ₃
D-penicillamine	+	+
Cystine	+	0
Penicillamine-cysteine disulphide	0	0
Penicillamine disulphide	0	0

TABLE II.—Correlation of Simple Tests with Results Obtained by Automatic Amino-acid Analysis

Patient	24-hour Urinary Cystine (mg.)	D-penicillamine R _s /q.d. (g.)	Nitroprusside Cyanide Test	FeCl ₃ Test†
P.C.*	360	—	2 ⁺⁺	—
	200	1	1 ⁺	—
	80	2	—	—

* Similar results were obtained in three other patients.

† No patient excreted significant amounts of free D-penicillamine.

Petechiae from Vests

Brit. med. J., 1965, 2, 521–522

A purpuric skin eruption is almost always significant and may indicate the presence of serious disorder. Only occasionally can spontaneous haemorrhages be disregarded—for example, the few scattered petechiae about the head and neck in a normal vertex delivery, the subconjunctival haemorrhage in whooping-cough, and the skin purpura of senility. A further entirely benign and common cause of petechiae in children, apparently not hitherto described, may therefore be of interest.

During the past year more than 50 children have been seen with small petechiae on the chest. After several had been investigated with entirely negative results, it became apparent that the petechiae often assumed a linear pattern corresponding

with that of “cellular” vests worn by the children, and it was then established that whenever petechiae were present a cellular vest was invariably worn. The haemorrhages were at times quite profuse (Fig. 1), but more often they were so scanty and tiny that only close scrutiny of the skin would reveal them. The commonest sites were over the lower ribs near the manubrium sterni, below the axillae, and posteriorly over the lower parts of the scapulae. The frequency with which these lesions occur in children who wear cellular vests is not known, but it is estimated that in more than a third of cases petechiae will be found if looked for carefully.

The petechiae caused no irritation whatsoever, and in fact were never noticed by the children or their parents. Associated erythema, papulation, or other skin changes were never seen. The vests worn were usually made locally by different firms, but the condition was also seen with time-honoured brand names from the United Kingdom. The material was either pure cotton, pure rayon, or mixtures of the two, all vests having in