creatinine clearance 2.1 ml./min.). The plasma electrolytes were: sodium 120, potassium 5.6, chloride 70, and bicarbonate 8 mEq/l. Her urine contained protein (0.5 g./l.) with a normal sediment, and was sterile on culture. A skeletal survey showed renal osteodystrophy with changes of hyperparathyroidism and rickets.

She was treated with intravenous saline and sodium bicarbonate with rapid improvement, and her blood urea fell to a minimum of 150 mg./100 ml. Subsequently she needed a high fluid intake, a diet restricted in protein, and an oral supplement of sodium bicarbonate.

The first radiological investigation of her urinary tract was a micturating cystogram. This showed a large (700 ml.) bladder which emptied normally. There was no ureteric reflex. Urography was then carried out with 60 ml. of sodium iothalamate (Conray 420) and immediate tomography. This showed normal-size kidneys with smooth outlines. The pelvicaliceal systems were faintly opacified but appeared normal. The most striking finding was the presence of numerous translucent cysts in the corticomedullary region (Figs. 1 and 2). The appearances were thought to be characteristic of medullary cystic disease.

COMMENT

Clinically this patient showed features typical of medullary cystic disease. The age of presentation, failure to conserve sodium and water, lack of hypertension, and the presence of severe renal failure with renal osteodystrophy are all characteristic, but not diagnostic. Among several conditions which may present in this way is familial juvenile nephronophthisis (Royer *et al.*, 1963), which is felt by some (Strauss and Sommers, 1967) to be pathologically indistinguishable, though a positive family history is found less often in medullary cystic disease (Strauss and Sommers, 1967). The condition is distinct from medullary sponge kidney (Strauss and Welt, 1963; Heptinstall, 1966), though several authors have confused the two conditions (Mulvaney and Collins, 1956; Lowen and Smythe, 1964). The main differences are in the age groups affected, in the course of the disease, and in the fact that the cysts in medullary cystic disease are at the corticomedullary junction (Strauss, 1962), while those in medullary sponge kidney are in the collecting ducts, and are at the tips of the papillae. Moreover, in medullary sponge kidney most nephrons are normal, while in medullary cystic disease the whole kidney is affected.

This would appear to be the first recorded example of the urographic diagnosis of this condition. The radiological changes are striking and seem to be diagnostic, since they

correspond exactly with the morbid anatomy. A case report by Faigel (1964) mentions normal appearances on retrograde pyelography, which is in accord with the pathological findings. The diagnosis can therefore be made only by using a urographic technique designed to demonstrate the renal parenchyma. High dosage of contrast and tomography are now recognized as being of value both in renal failure (Schwartz *et al.*, 1963) and in patients with suspected abnormalities of the renal parenchyma (Saxton, 1968). In the subject with renal failure, as in the normal subject, the nephrogram shows continuous improvement with increasing dosage after opacification of the collecting systems has ceased to show any increase (Doyle *et al.*, 1967). Thus abnormalities of the parenchyma may be demonstrable in renal failure, and the case described above is an excellent example of the diagnostic value of this method.

We would like to thank Dr. T. S. Rogers, of Margate General Hospital, who referred this patient to us.

Requests for reprints to be sent to Dr. C. S. Ogg.

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REFERENCES

- Doyle, F. H., Sherwood, T., Steiner, R. E., Breckenridge, A., and Dollery, C. T. (1967). *Lancet*, 2, 964.
Faigel, H. C. (1964). *Amer. J. Dis. Child.*, 107, 277.
Heptinstall, R. H. (1966). *Pathology of the Kidney*, p. 93. London.
Lowen, W., and Smythe, A. D. (1964). *Clin. Radiol.*, 15, 271.
Mulvaney, W. P., and Collins, W. T. (1956). *J. Urol.*, 75, 776.
Royer, P., Habib, R., and Mathieu, H. (1963). *Problèmes Actuels de Néphrologie Infantile*, p. 250. Paris.
Saxton, H. M. (1968). *Proc. roy. Soc. Med.*, 61, 27.
Schwartz, W. B., Hurwit, A., and Ettinger, A. (1963). *New Engl. J. Med.*, 269, 277.
Strauss, M. B. (1962). *Ann. intern. Med.*, 57, 373.
Strauss, M. B., and Sommers, S. C. (1967). *New Engl. J. Med.*, 277, 863.
Strauss, M. B., and Welt, L. G. (1963). *Diseases of the Kidney*, p. 938. London.

Malabsorption Induced by Para-aminosalicylate

Brit. med. J., 1969, 1, 825-826

Oral para-aminosalicylate (P.A.S.) is often associated with gastrointestinal disturbances, and, though diarrhoea is not uncommon (Goodman and Gilman, 1965), frank steatorrhoea is not usually recognized in clinical practice. Oral P.A.S., however, has been shown to increase faecal fat excretion experimentally in normal subjects (Levine, 1968). The following report is that of a patient who received P.A.S. and isoniazid therapy for tuberculosis and developed steatorrhoea, which remitted when the P.A.S. was stopped.

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CASE REPORT

In 1946 a brewery clerk aged 33 underwent a Polya partial gastrectomy for peptic ulcer. In 1965 an iron-deficiency post-gastrectomy anaemia was diagnosed. As the serum vitamin B₁₂ concentration was low cyanocobalamin was given in addition to oral iron therapy. In February 1968 he developed a left pleural effusion. Pleural biopsy suggested tuberculosis. In view of an admitted high alcohol intake and abnormal liver function tests liver biopsy was performed, which showed early cirrhosis and disseminated tuberculosis. Antituberculous therapy was started with anhydrous sodium P.A.S. 12 g. and isoniazid 300 mg. daily as Inapasade granules. After 12 weeks' treatment he developed frequent blood-stained semi-formed stools. On readmission in June, after 15 weeks' therapy, he had a distended abdomen with visible painless peristalsis. The bowels were open 10 times a day, stools being characteristic of steatorrhoea and streaked with blood and mucus. The pleural

effusion had resolved. A diet containing 70 g. fat was started, and after investigation P.A.S. was withdrawn and streptomycin (1 g.) intramuscularly on alternate days given. Isoniazid was continued. Within seven days of the discontinuance of P.A.S. the stools had become macroscopically normal and remained so.

In 1965 the haemoglobin was 10 g./100 ml.; serum iron 19 µg./100 ml.; vitamin B₁₂ 4.6 µg./ml.; and folate 17.5 mµg./ml. The chest x-ray picture was normal.

In February 1968 (before P.A.S.) chest x-ray examination showed left pleural effusion; the haemoglobin was 13.7 g./100 ml.; serum urea 23 mg./100 ml., bilirubin 0.7 mg./100 ml., alkaline phosphatase 19 K.A. units/l., aspartate aminotransferase 212 units/l., iron 57 µg./100 ml., and unsaturated iron-binding capacity 340 µg./100 ml. Bromsulphalein retention was 9% at 45 minutes. Pleural fluid: protein content 4.8 g./100 ml., many lymphocytes, no malignant cells. Pleural biopsy: granulation tissue containing epithelioid and giant cell foci suggestive of tuberculosis. Liver biopsy: fatty infiltration, early fibrosis, and two small epithelioid foci suggestive of disseminated tuberculosis. Barium meal examination: small gastric remnant, flocculation pattern in small bowel, no abnormality on follow-through examination.

In June 1968 (on P.A.S.) the haemoglobin was 11.1 g./100 ml.; serum iron 48 µg./100 ml.; bilirubin 0.2 mg./100 ml., alkaline phosphatase 16 K.A. units/l., aspartate aminotransferase 60 units/l., and cholesterol 132 mg./100 ml. Serum salicylate levels after oral dose of 6 g. of P.A.S.: 1 hour, 10 mg./100 ml.; 2 hours, 11 mg./100 ml.; 3 hours, 9 mg./100 ml.; 4 hours, 6 mg./100 ml.; 12 hours, none detectable. Sigmoidoscopy showed mild haemorrhagic granular proctitis. Chest x-ray examination showed pleural thickening of left base. Barium meal test, unchanged from February. Barium enema normal. Sternal marrow: iron deficiency and megaloblastic changes. Jejunal biopsy normal. Jejunal intubation (Lundh, 1962; Wiggins, 1967): trypsin content of jejunal juice after Lundh meal 3.5 µEq/ml./min. Bile salts showed neither deconjugation nor precipitation on addition of P.A.S.; bacterial flora normal (staphylococci count 7.2×10^3 /ml. *Proteus mirabilis* count 3.3×10^3 /ml.).

Results of studies during P.A.S. therapy and after its withdrawal are shown in the Table.

Studies Before, During, and After P.A.S. Therapy

	February 1968	June 1968			Normal Range
		On P.A.S.	Off P.A.S.	Days Off P.A.S.	
*Faecal fat (g./24 hours) ..	1.0	12.2	6.4 4.3 2.1	4-6 7-9 10-12	> 6
†Faecal weight (g./24 hours) ..	—	547	168 210	7-12 18-23	
‡ ⁵⁷ Co vitamin B ₁₂ absorption (with intrinsic factor) ..	—	43%	77%	32	> 50%
§Serum folate (mµg./ml.) ..	6.6	1.7	2.7	5	4-18
§Xylose absorption:					
Blood level at 90 min. (mg./100 ml.) ..	—	23	89	33	> 32
Urine excretion in 5 hours (g.) ..	—	1.8	8.3	33	> 5
Total serum protein ..	6.9	4.7	6.3	30	6.2-8
Albumin (g./100 ml.) ..	3.6	2.5	3.3	30	3.8-5
Serum calcium (mg./100 ml.) ..	—	7.9	10.1	30	9-10.5

* Mean of 3 days on 70-g. fat intake.

† Mean of 5 days.

‡ Faecal excretion method of Mollin and Waters (1968): ⁵⁷Co-labelled vitamin B₁₂ administered orally.

§ After oral dose 25-g. D-xylose.

COMMENT

The appearance of steatorrhoea soon after starting P.A.S. therapy and the rapid amelioration after its withdrawal suggest

that P.A.S. was the direct cause of the malabsorption. Furthermore, with concurrent intrinsic factor administration the vitamin B₁₂ malabsorption was present only during the P.A.S. treatment and therefore was not due to the gastrectomy. However, the interaction of the effects of the gastrectomy and the P.A.S. probably accounts for the florid steatorrhoea in this patient. Therapeutically effective serum salicylate concentrations were obtained despite the malabsorption. In the absence of significant anorexia the folate and protein deficiencies are more likely to be the result of the enteropathy than malnutrition. A tuberculous enteritis can be excluded by the normal barium follow-through examination and negative intestinal biopsy.

The mechanism of the P.A.S.-induced malabsorption is not clear. Unlike the effects of neomycin, there were neither morphological changes in the jejunal biopsy nor precipitation of the bile salts (Faloon *et al.*, 1967; Dobbins *et al.*, 1968). The bacterial flora was unaltered and the trypsin content of the jejunal juice was not reduced to the levels seen when steatorrhoea is associated with pancreatic insufficiency (Cook *et al.*, 1967).

Heinivaara *et al.* (1964) and Heinivaara and Palva (1964, 1965) reported mild vitamin B₁₂ and xylose malabsorption in tuberculous patients on P.A.S., but the only reports of increased faecal fat excretion appear to have been by Tygstrup *et al.* (1961) and Levine (1968), who demonstrated this effect in normal subjects given test doses of P.A.S. It appears that P.A.S. should be added to the list of drugs which may induce frank reversible malabsorption in clinical practice.

I am grateful to Professor E. F. Scowen for permission to publish this case; to Dr. G. M. Besser for advice; to Dr. A. M. Dawson and his gastroenterological unit for intubation studies and jejunal biopsy; and to Dr. A. H. Waters, department of haematology, for the vitamin B₁₂ absorption studies.

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REFERENCES

- Cook, H. B., Lennard-Jones, J. E., Sherif, S. M., and Wiggins, H. S. (1967). *Gut*, **8**, 408.
- Dobbins, W. O., Herrero, B. A., and Mansbach, C. M. (1968). *Amer. J. med. Sci.*, **255**, 63.
- Faloon, W. W., Paes, I. C., Woolfolk, D., Nankin, H., Wallace, K., and Haro, E. N. (1966). *Ann. N.Y. Acad. Sci.*, **132**, 879.
- Goodman, L. S., and Gilman, A. (1965). *The Pharmacological Basis of Therapeutics*, 3rd ed. London.
- Heinivaara, O., and Palva, I. P. (1964). *Acta med. scand.*, **175**, 469.
- Heinivaara, O., and Palva, I. P. (1965). *Acta med. scand.*, **177**, 337.
- Heinivaara, O., Palva, I. P., Siurala, M., and Pelkonen, R. (1964). *Ann. Med. intern. Fenn.*, **53**, 75.
- Levine, R. A. (1968). *Ann. intern. Med.*, **68**, 1265.
- Lundh, G. (1962). *Gastroenterology*, **42**, 275.
- Mollin, D. L., and Waters, A. H. (1968). *The Study of Vitamin B₁₂ Absorption using Labelled Cobalamines*, Med. Monogr. No. 6. Amersham.
- Tygstrup, N., Winkler, K., and Jørgensen, K. (1961). *Ugeskr. Læg.*, **123**, 255.
- Wiggins, H. S. (1967). *Gut*, **8**, 415.