calcification. By 1963 Punsar and Somer were able to review 33 reported cases of irreversible renal failure due to prolonged excessive intake of absorbable alkali, associated in most but not all instances with excessive milk consumption.

Rifkind *et al.* (1960) reported the only previous British case that we have been able to find with the principal features of the chronic milk-alkali syndrome. Their patient was a woman of 48 who had taken 30 Rennies tablets daily for 10 years without excessive milk intake. Besides uraemia and nephrocalcinosis there were calcium deposits in the corneae and sclerae, aorta, and abdominal lymph nodes and there was generalized osteosclerosis, whereas our patient had radiologically normal bones. Our case, like theirs, had an excessive intake of calcium and absorbable alkali derived from Rennies tablets. In our patient the rapid fall in the serum calcium level with subsequent improvement in the general state of health and fall in blood urea after stopping the Rennies tablets indicates that they were the cause of the hypercalcaemia and nephrocalcinosis. The absence of further deterioration of renal function almost three years after stopping the tablets is noteworthy. Both our patient and that of Rifkind *et al.* took large quantities of Rennies

tablets because they had developed a liking for them. It seems improbable that any patient would take so many antacid tablets solely to relieve dyspepsia.

We are grateful to Dr. J. D. N. Nabarro for advice. We wish to thank Dr. H. L. Marriott for permission to report this case.

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REFERENCES

- Burnett, C. H., Commons, R. R., Albright, F., and Howard, J. E. (1949). *New Engl. J. Med.*, **240**, 787.
Cope, C. L. (1936). *Clin. Sci.*, **2**, 287.
Punsar, S., and Somer, T. (1963). *Acta med. scand.*, **173**, 435.
Rifkind, B. M., Chazan, B. I., and Aitchison, J. D. (1960). *Brit. med. J.*, **1**, 317.

Pernicious Anaemia and Intestinal Malabsorption: Spinal Cord Degeneration Developing during Vitamin B₁₂ Treatment

Brit. med. J., 1967, **3**, 657-658

CASE REPORT

The patient was born in Northamptonshire in 1890 and emigrated to New Zealand at the age of 33. In 1927, when aged 37, she began to pass loose pale stools, about six daily. She complained of audible bowel sounds and of excessive flatus. When first seen by a physician she was aged 59 and considerably underweight. Severe macrocytic anaemia and a megaloblastic sternal marrow were present. Gastric analysis showed achlorhydria. Her pale stools, when dried, contained 32% by weight of fat. A barium enema was normal. Her blood picture quickly returned to normal after the twice-weekly injection of Anahaemin (liver extract) 2 ml. As diarrhoea continued in spite of a low-fat diet, folic acid 10 mg. b.i.d. was added, but was soon discontinued because her diarrhoea increased. Fortnightly injections of Anahaemin were continued, given by her general practitioner.

She was not seen again by a physician until the age of 66. Her blood was then normal, with a packed cell volume of 40%. Her stools were still pale and loose, and contained 36% by weight of fat. Her glucose tolerance curve was flat. A gluten-free diet was started and cortisone acetate 25 mg. was given by mouth twice daily. She improved in health, her diarrhoea diminished, and she was able to take a trip to the United Kingdom.

At the age of 69 she was still in good health, with one stool daily. Liver extract injections were then stopped, and vitamin B₁₂ 200 µg., weekly at first and later fortnightly, was prescribed. The gluten-free diet and cortisone were continued.

At the age of 70 she was found on routine examination to have reduced vibration sense in both lower legs. Later in the same year she complained of unsteadiness of gait, and there was some oedema of both legs. Her blood count and serum proteins were normal.

The following year she became increasingly unsteady on her feet, especially when walking in the dark. She complained of weakness of her legs and of tingling burning sensations in both feet and to a lesser extent in her hands. Examination revealed a positive Romberg sign, an ataxic gait, and some impairment in her legs of all sensory modalities, especially vibration and postural sensibility.

Both knee and ankle jerks were abnormally brisk and the plantar reflexes were extensor. The clinical picture was that of subacute combined degeneration of the cord with mild peripheral neuritis.

In view of this development the vitamin B₁₂ dosage was increased to 200 µg. twice weekly and she was admitted to hospital for reassessment. Repeated peripheral blood counts and a sternal marrow examination were normal. Repeated serum vitamin B₁₂ levels were well within the normal range—namely, 460 and 480

FIG. 1.—Barium-meal examination showing multiple small-bowel diverticula.

µg./ml. (normal 150-650). Her serum folic acid was 8 µg./ml. (normal 5-16). Augmented histamine stimulation failed to provoke any gastric secretion of hydrochloric acid. Absorption of cobalt-labelled vitamin B₁₂ (Schilling test) was grossly defective. This absorption test was repeated after the administration of

intrinsic factor, and though there did seem to be slight improvement this was not thought to be significant. A xylose-absorption test gave an abnormally low result. Her renal function was normal.

A barium-meal examination showed three large diverticula of the duodenum and numerous smaller ones of the proximal jejunum. In the lower jejunum and ileum the barium became flocculated with a typical malabsorption pattern which made demonstration of diverticula impossible in this region.

She was given a prolonged oral course of tetracycline without obvious clinical improvement. Vitamin B₁₂ 200 µg. was administered thrice weekly and her serum B₁₂ level rose to 1,080 µg./ml. In addition thiamine hydrochloride 100 mg. was given intramuscularly each day. As there was no obvious improvement in her condition vitamin B₁₂ was later discontinued and a change made to Neo-hepatex 2 ml. twice weekly for a period of eight months. There was still no

FIG. 2.—Necropsy specimen of small bowel showing diverticulosis.

obvious improvement, so the frequency of administration was reduced to once a week and eventually to once a fortnight.

By this time she was leading a wheel-chair existence because of her ataxia and weakness. Her nervous system signs remained much the same, except that her ankle reflexes were now less brisk than her knee reflexes. She remained in this state, with little progression, during the next four years, and throughout this time she was mentally alert. She then had an attack of persistent vomiting and was admitted to hospital in a state of shock. Her abdomen was distended, and bowel sounds were diminished, though there was an absence of pain or tenderness. Colon bacilli were cultured from her blood. In spite of intensive restorative measures she died. She was then aged 76.

Necropsy Report.—Stomach: thin-walled. Duodenum: three large diverticula of the second part. Jejunum-ileum: numerous large, wide-mouthed, slightly loculated mesenteric diverticula gradually diminishing in number and size to the mid-gut, but still present

though smaller, to the terminal ileum; ulceration of Peyer's patches in lower end of ileum, one of them on the point of perforation. Brain: weight 920 g.; considerable gyral atrophy with focal atrophy of the cerebellum. Spinal cord: general atrophy. Bones: well-marked vertebral osteoporosis.

Microscopical Findings.—Stomach: complete gastric atrophy with reversion to a "colonic" type of mucosa; muscle also thin. Jejunum-ileum: villous structure preserved. Liver: fatty change

FIG. 3.—Section of spinal cord showing dorsal and lateral tract degeneration.

associated with peliosis. Brain: no gross neuronal "fall-out" in cortex or brainstem nuclei. Spinal cord: degeneration of dorsal and lateral columns typical of subacute combined degeneration.

COMMENT

This unusual case in which symptoms and signs of spinal cord degeneration appeared while the patient was receiving adequate parenteral vitamin B₁₂ or liver extract was about to be reported when Ellis, Breuer, Owen, and Laszlo (1966) reported a similar experience. In the present case, however, the clinical findings were supported by post-mortem examination.

This patient undoubtedly suffered from pernicious anaemia. In addition, there was evidence of intestinal malabsorption apparently related to her extensive small-bowel diverticulosis. Subacute combined degeneration progressed in spite of an increase in dosage of vitamin B₁₂ and also of a reversion to liver extract. Serum vitamin B₁₂ was normal at a time when her condition was progressing and there was no improvement even when her serum B₁₂ level was raised to twice normal levels.

It would appear, therefore, that here as in the case reported by Ellis *et al.* (1966) the patient's nervous system was unable to utilize vitamin B₁₂.

I am grateful to the medical superintendent, Christchurch Hospital, Dr. W. I. Paterson, for permission to publish this case and to the director of pathology, Dr. D. T. Stewart, and the assistant radiologist, Dr. R. H. Gibson, for their help.

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REFERENCE

- Ellis, G. J., Breuer, R. I., Owen, E. E., and Laszlo, J. (1966). *Ann. intern. Med.*, 64, 654.