

Vitamin B₁₂ absorption after resection of ileum in childhood

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Valman, H. B., and Roberts, P. D. (1974). *Archives of Disease in Childhood*, 49, 932. **Vitamin B₁₂ absorption after resection of ileum in childhood.** Impaired absorption of vitamin B₁₂ has been shown by a whole body counter technique in 7 of 10 infants and children who had resection of over 45 cm of ileum. Absorption was normal in 2 patients who had 15 cm or more terminal ileum remaining. If absorption was abnormal the serum level of vitamin B₁₂ did not fall below the lower limit of the normal range for several years, puberty being a particularly vulnerable time. Though the site and length of the resection often suggested whether vitamin B₁₂ deficiency was likely to occur, an absorption test was necessary for accurate prediction and to allow treatment to be given rationally before complications occurred. The whole body counter technique was particularly suitable for children as it did not involve collection of urine or faeces, injections, or admission to hospital.

There have been only four reports of malabsorption of vitamin B₁₂ after resection of ileum in childhood (Clark and Booth, 1960; Dallman and Diamond, 1960; Helge, 1962; Valman, 1972). A large part of the jejunum as well as the whole ileum was resected in the first 2 cases and a low serum vitamin B₁₂ level was discovered within 4 years of the resections. The last patient developed vitamin B₁₂ deficiency for the first time during puberty. We have studied a total of 12 patients who had resections of various lengths of ileum, to determine the importance of the length and site of the resection and the interval before vitamin B₁₂ deficiency was likely to occur. In 10 of these patients vitamin B₁₂ absorption was studied by the whole body counter technique.

Patients and methods

Details of the patients studied are in the Table. The resections in Cases 1-8 were performed in the neonatal period, Case 9 had resections at 1.5 and 2.5 years, Case 10 at 3.3 years, Case 11 at 4.8 years, and Case 12 at 10 years.

Haematological methods were standard (Dacie and Lewis, 1968). Serum vitamin B₁₂ was assayed using *Euglena gracilis* strain Z (Anderson, 1964). The normal range is 160-925 ng/l. Serum folate was measured using *Lactobacillus casei* (Waters and Mollin, 1961). The normal range by this method is 6-21 µg/l., but in patients

with megaloblastic anaemia due to folate deficiency the levels are usually below 3 µg/l., together with low red cell folate levels. Red cell folate levels were measured by estimating the *L. casei* activity of haemolysates of sequestrenized whole blood samples (Hoffbrand, Newcombe, and Mollin, 1966), the normal range being 160-640 µg/l. packed red cells. Serum iron and iron binding capacity were estimated by the method of Zak and Ressler (1956) and the normal range of serum iron is 14.3-26.8 µmol/l.

Vitamin B₁₂ absorption was determined using an oral dose of 1 µg ⁵⁸Co-labelled vitamin B₁₂ plus intrinsic factor and the whole body counting technique (Callender *et al.*, 1966). In our experience normal adults absorb at least 40% of the dose. For children below the age of 12 years the radiation dosage was reduced by giving 0.5 µg ⁵⁸Co-labelled vitamin B₁₂ together with 0.5 µg of unlabelled vitamin B₁₂, plus intrinsic factor. After an overnight fast the patient lay on a couch which moved past a counter over approximately 10 minutes. Using the 'shadow shield' whole body counter, the patient is not enclosed and this enables the mother to stand next to the child throughout the procedure. The dose of vitamin B₁₂ with intrinsic factor was given in a glass of water and the patient was counted again. He returned home fasting for at least a further 3 hours. A final count was performed a week later and the retention calculated.

Results

In 7 patients with less than 15 cm of terminal ileum remaining vitamin B₁₂ absorption was abnormal, less than 20% in 6 and 28% in one patient

TABLE
Clinical details and results of investigations

Case no.	Reason for resection	Period since resection (yr)	Small gut left (cm at laparotomy)	Small gut removed (cm fixed specimen)	Terminal ileum left (cm at laparotomy)	Serum vitamin B ₁₂ (ng/l.)	Vitamin B ₁₂ absorption with intrinsic factor (% of dose retained)
1	Multiple atresia	14	—	53	30	200	77
2	Volvulus malrotation	13	—	67	15	624	72
3	Atresia	13	—	65	0	268*	4
4	Volvulus malrotation	7	65	90	12	272	28
5	Volvulus duplication	6	65	100	2	380	—
6	Volvulus atresia	5	80	73	0	221	12
7	Septum	5	78	48	10	264	18
8	Volvulus malrotation	1	40	125	26	762	—
9	Long segment Hirschsprung's disease	4, 5	—	28 + 65	0	216	39
10	Volvulus malrotation	4	127	220	7	160	0
11	Sickle cell disease	1	—	130	2	588	18
12	Tuberculosis + stagnant loop	2	155	81	0	415*	4

*Receiving i.m. vitamin B₁₂.

(Table and Fig. 1). Absorption was normal (77% and 72%) in 2 patients with 15 and 30 cm of terminal ileum. One patient (Case 9) absorbed 39% of the oral dose of vitamin B₁₂, which is borderline normal. This patient had two resections, the second at 2½ years, and a large amount of mid to lower ileum may have been preserved.

Two cases had had injections of vitamin B₁₂ and

their serum levels were normal. The serum vitamin B₁₂ level of Case 10 was borderline (160 ng/l.); in the remaining 9 cases the serum vitamin B₁₂ levels were well within the normal range (200–762 ng/l.).

In Case 3 the serum vitamin B₁₂ level was normal until puberty when it fell precipitously over 6 months to 72 ng/l. (Fig. 2). At this time the blood

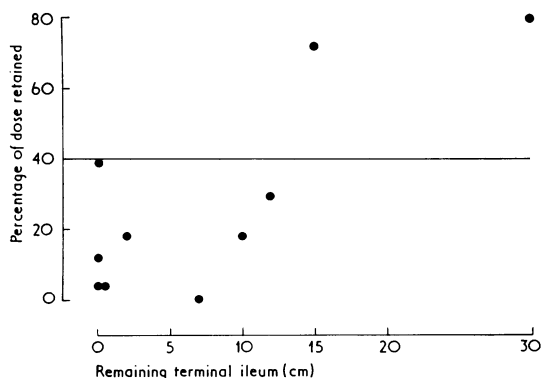


FIG. 1.—Relation of vitamin B₁₂ absorption to the length of remaining terminal ileum in 10 children. Normally absorption is >40%.

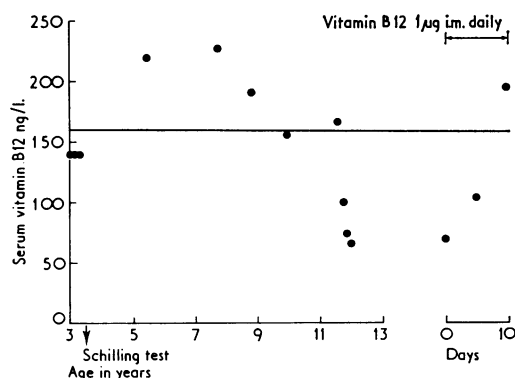


FIG. 2.—Serum vitamin B₁₂ levels in Case 3 between the ages of 3 and 11½ years. Serum vitamin B₁₂ levels when physiological doses of vitamin B₁₂ were given at 11½ years.

film showed normal red cells, with no macrocytosis and no hypersegmented neutrophils.

Case 2 had folate deficiency, the serum folate was 3.8 µg/l. and red cell folate 153 µg/l. Case 11 had sickle cell disease, was anaemic, and had a serum folate of 2.0 µg/l. All the remaining patients had normal haemoglobin and serum folate levels. The serum iron level was 9.0 µmol/l. in Case 6 and 8.0 µmol/l. in Case 7, but the serum iron binding capacities were normal. The serum iron levels were normal in the remaining patients.

Discussion

Length of resection. Booth (1963) found that in adults vitamin B₁₂ absorption was normal when less than 60 cm of ileum were removed but was usually impaired when 180 cm or more were removed. Fone *et al.* (1961) concluded that vitamin B₁₂ absorption was normal after resection of less than 30 cm and usually impaired when a greater length was removed, though it was normal in one patient who had lost as much as 120 cm. In most of these patients resection was performed for regional enteritis, the terminal ileum was removed and possibly some of the remaining bowel was abnormal.

The present study confirms that after neonatal resection of the ileum, the remaining small bowel does not absorb adequate amounts of vitamin B₁₂. It is not possible to calculate the corresponding lengths of intestine resected in comparison with the adult, as patients with congenital abnormalities, which were present in 9 of these 12 patients, often have an abnormally short small intestine (Valman, 1973). Vitamin B₁₂ absorption was normal where approximately 15 cm of the most terminal part of the ileum was preserved (Cases 1 and 2 and 2 patients reported by Moe, 1964, and Benson, Lloyd, and Krabbenhoft, 1967) and was impaired where a shorter length remained (Fig. 1). Impaired absorption cannot be predicted from the length of intestine resected, as illustrated by Case 9, but the length of the remaining gut is a guide to absorptive capacity. However, some surgeons have considered that the handling of the gut necessary for careful measurement is not justifiable as a routine procedure in such extremely ill babies.

Site of resection. The impaired vitamin B₁₂ absorption in Cases 7 and 12, who both have some proximal ileum, confirmed at the original operation, shows that the distal ileum is necessary for normal vitamin B₁₂ absorption. The normal absorption of vitamin B₁₂ in Case 2 and the low absorption in Case 3, who had similar lengths but different sites of resection, also confirm that the distal ileum is the most important site for vitamin B₁₂ absorption.

Interval before serum vitamin B₁₂ level falls.

In adults after total gastrectomy the serum vitamin B₁₂ level may not fall for 10 years due to large stores in the liver (Booth, 1963). Even in adults where absorption may be virtually nil after ileal resection, as long as 6 years have elapsed before the serum vitamin B₁₂ level has fallen (Booth, 1963). In two reports of low serum vitamin B₁₂ levels due to resection of the ileum in childhood (Clark and Booth, 1960; Dallman and Diamond, 1960) subnormal levels were reached within 4 years of the resection. Booth (1961) warned that in children low serum vitamin B₁₂ levels might occur at a shorter interval after resection than in adults, and Küffer *et al.* (1965), who reviewed all the previous reports of major resections in childhood, were surprised that their patient had not developed megaloblastic anaemia by 17 months after resection of the ileum.

In Case 3 (Fig. 2), after three slightly subnormal serum vitamin B₁₂ levels between 3 and 3½ years, the level remained well within the normal range until the age of 10 years. After a further year at borderline levels there was a precipitate fall to 72 pg/l. over a period of 6 months during the pubertal growth spurt. Helge (1962) described a 13-year-old girl with megaloblastic anaemia due to vitamin B₁₂ deficiency 5 years after resection of 80 cm of the terminal ileum but our patient did not develop megaloblastic anaemia. The pubertal stage of the patient described by Helge was not mentioned. The only supplementary dose of vitamin B₁₂ Case 3 had received was 1 mg intramuscularly during a Schilling test at the age of 3½ years and about 150 µg of this dose would have been retained (Chanarin, 1969).

Three children in the present series still have normal serum vitamin B₁₂ levels over 5 years after resections of ileum despite impaired absorption of vitamin B₁₂.

Three patients were investigated in detail for evidence of a stagnant loop (Cases 3, 4, and 10). In all three there was no evidence of a stagnant loop on barium meal and follow through, and aerobic and anaerobic cultures of the small gut contents showed no significant growth of pathogens. Urinary indicans were estimated in Cases 3 and 10 and were normal (64 and 23 µg/24 hours). Fat excretion was not decreased by oral antibiotics in the two patients tested (9.1–9.3 g/day in Case 4; 14.1–24.6 g/day in Case 10).

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