

Absorption of vitamin B₁₂ in tobacco amblyopia

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In view of the evidence that some abnormality of the metabolism of vitamin B₁₂ is present in tobacco amblyopia (Callender and Denborough, 1957; Heaton, McCormick, and Freeman, 1958; Chisholm, Brontë-Stewart, and Foulds, 1967), it was thought possible that absorption of the vitamin might be reduced in patients with the disease.

The patients studied were male pipe smokers with bilateral acquired defects of visual acuity, bilateral centrocaecal scotomata, and defective colour discrimination resembling that found in deuteranopia. Examinations of blood, bone marrow, and serum vitamin B₁₂ were done on all patients. No patient in this series showed evidence of megaloblastic haemopoiesis, and patients with pernicious anaemia or any other type of malabsorption were excluded as it was felt that such cases already had an adequate cause for B₁₂ deficiency. (In our whole series of cases of tobacco amblyopia, we have the impression of a relatively high incidence of pernicious anaemia, partial gastrectomy, or diabetes mellitus compared with the incidence expected in a control sample of the population. However, it would not be justified to deduce that all cases of tobacco amblyopia therefore had a similar defect in absorption or metabolism of vitamin B₁₂; hence our decision to study in isolation the group of cases without the associated conditions.)

Part I

Initially, the intestinal absorption of vitamin B₁₂ was assessed in fifteen patients (eleven aged 30–69 years and four aged over 70 years) by means of the Schilling test (Schilling, 1953). After a fast of 12 hours, 1 µg. of 1 µCi ⁵⁸Co-labelled vitamin B₁₂ was given by mouth, followed one hour later by 1 mg. cyanocobalamin intramuscularly. The amount of labelled B₁₂ excreted in a 24-hour collection of urine was expressed as a percentage of the oral dose. All Schilling tests were done in the same laboratory by the same observer.

The results in patients with tobacco amblyopia were compared with those obtained in a series of 120 males without haematological or biochemical evidence of pernicious anaemia, of whom 96 were aged 30–69 years and 24 were over 70 years of age.

RESULTS (Table I, overleaf)

The values obtained in tobacco amblyopia lie within the normal range with the exception of Case 7; the value obtained in this case is probably explained by the errors in the method, which is admittedly rather imprecise.

Table I Results of Schilling tests in 15 patients with tobacco amblyopia and 120 controls

Patient No.	Age (yrs)	Vitamin B ₁₂ excretion*		
		Per cent. of oral dose	Range	Mean
1	45	15		
2	49	12		
3	52	17		
4	55	20		
5	55	11.2	6.5-20	13.4
6	59	18	(7.3-32)	(16.4)
7	60	6.5		
8	60	11		
9	63	8.4		
10	65	19		
11	66	8.8		
12	70	22.7		
13	72	7.4	7.3-24	15.4
14	82	7.3	(6.3-19)	(15.1)
15	84	24		

* Mean and range of vitamin B₁₂ excretion for the 120 controls shown in brackets

Part II

An extension of this study was prompted by the observation that absorption of folic acid is diminished when it is ingested simultaneously with diphenylhydantoin (Epanutin) (Dahlke and Mertens-Roesler, 1967). This suggested the possibility that smoking might have a similar effect on the absorption of vitamin B₁₂ in tobacco amblyopia. The Schilling test was performed on seven patients with tobacco amblyopia who had not succeeded in giving up smoking, under two different circumstances

- (a) after abstaining from smoking for 12 hours before and during the test.
- (b) after an interval of 2 days, the patient being encouraged this time to smoke during the test, and especially between the oral and intramuscular doses of vitamin B₁₂. Patients 1, 3, 5, and 6 smoked during the first of their two Schilling tests; Patients 2, 4, and 7 during the second of their two tests.

RESULTS

In all seven patients, the percentage of the oral dose of radioactive B₁₂ excreted in the urine in 24 hours was lower when the patients smoked during the test than when they did not (although in Patient 1 the fall was minimal); see the Figure and Table II (opposite). With a non-parametric (sign) test, $P = 0.015$. By Student's "t" test $t = 3.35$; $n = 6$; $0.025 > P > 0.01$. Both these statistical criteria indicate a significant difference in excretion at the 2 per cent. level of probability, which is presumably due to diminished absorption when the patient smoked during the Schilling test.

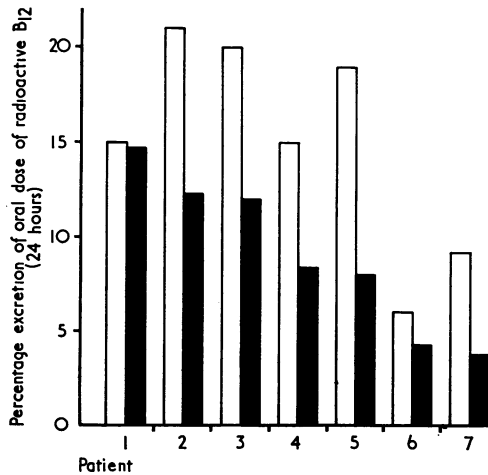


FIGURE Percentage excretion of oral dose of vitamin B₁₂ in seven patients

□ Not smoking ■ Smoking

Note lower excretion (and presumably absorption) when patients smoke

Table II Schilling tests with and without smoking in 7 patients

Patient No.	Age (yrs)	Vitamin B ₁₂ excretion (per cent. of oral dose)	
		Not smoking	Smoking
1	46	15	14.9
2	50	21.4	12.3
3	54	20	12
4	63	15	8.4
5	65	19	8
6	46	6	4.2
7	72	9.3	3.8

Discussion

The normal results of the standard Schilling test found in the first 15 patients with tobacco amblyopia (see para. 4 above, and Table I) do not exclude the possibility that some abnormality might be revealed if B₁₂ absorption were studied by methods more sensitive than the Schilling test. Nevertheless, the depression of B₁₂ excretion, and therefore presumably of absorption, when patients smoke, might be significant in explaining the pathogenesis of tobacco amblyopia. In general, smokers are most likely to indulge in the habit shortly after a meal, and this might depress the absorption of the vitamin, most directly because of a swallowed toxin such as cyanide but also possibly through the effect of a toxin which might be absorbed in the mouth or lungs and carried in the bloodstream to the stomach, perhaps reducing the affinity of intrinsic factor for B₁₂. In support of the latter hypothesis, there is an observation in mice (Clemenson, Sörbo, and Ullberg, 1960) that *injected* radioactive cyanide and thiocyanate are found in high concentration in the gastric mucosa; an affinity for the submaxillary salivary glands was also observed, so that a rather remote possibility is that some such toxin in tobacco might similarly be concentrated in the lacrimal gland and secreted in tears, and might then be absorbed through the cornea into the eye to exert a local effect on the retina (see MacKenzie and Phillips, 1968; Phillips, Ainley, Van Peborgh, Watson-Williams, and Bottomley, 1968).

Summary

In fifteen patients with tobacco amblyopia (excluding those with pernicious anaemia and partial gastrectomy), absorption of vitamin B₁₂ as measured by the Schilling test was not abnormally low. Schilling tests performed in a further seven patients showed that, when they smoked during the test, excretion (and presumably absorption) of vitamin B₁₂ was less in all cases than when they did not smoke (although the difference was minimal in one case).

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