a comparison of measles virus and poliovirus type 2 serum/C.S.F. ratios in these three cases of subacute sclerosing panencephalitis that measles antibody may be produced or released within the central nervous system. The poliovirus type 2 neutralizing antibody, which acted as an indicator of an intact blood-brain barrier, would be contained in the IgG and IgA fractions. Measles IgM and IgG were present in the C.S.F. of these three patients whereas neither was detected in the C.S.F. of five "normal" patients. The presence of any measles IgM in the C.S.F. is abnormal, since IgM has not been detected in normal C.S.F. (Cohen and Bannister, 1967; Merrill, Hartley, and Claman, 1967). The measles IgG serum/C.S.F. ratio was lower than the poliovirus type 2 serum/C.S.F. ratio in the three patients with subacute sclerosing panencephalitis. These results suggested that both measles IgM and IgG may be produced within the central nervous system. It is unlikely that much antibody was derived from cells in the C.S.F., since the cell count in the three cases was within normal limits.

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Intrinsic-factor Antibody and Absorption of Vitamin B₁₂ in Pernicious Anaemia

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Summary

The mean urinary excretion in a vitamin-B₁₂ absorption (Schilling) test in control subjects was 19.2% and in pernicious anaemia when given with additional intrinsic factor was as follows: no intrinsic-factor antibodies demonstrable 19.3%, antibodies in serum only 14.4%, antibodies in gastric juice only 11.1%, and antibodies in both serum and gastric juice 8.4%. It is concluded that intrinsic-factor antibody exerts an adverse effect on vitamin-B₁₂ absorption in most patients with pernicious anaemia.

Introduction

The antibody to gastric intrinsic factor present in serum in just over half the patients with pernicious anaemia prevents the binding of vitamin B₁₂ to intrinsic factor. When serum containing such an antibody is given orally with vitamin B₁₂ it interferes with the absorption of the vitamin mediated by intrinsic factor (Schwartz, 1960). Nevertheless, vitamin-B₁₂ absorption (with added intrinsic factor) was found to be essentially the same in those patients with pernicious anaemia who had a demonstrable serum intrinsic-factor antibody and those without (Ardeman and Chanarin, 1965; Yates and Cooper, 1967).

A few cases have been recorded where free antibody to intrinsic factor was present in the gastric secretion associated with impaired absorption of vitamin B₁₂ when given with added intrinsic factor (Schade, Feick, Muckerheide, and Schilling, 1966; Herbert, Carmel, and Li, 1967). Antibody to intrinsic factor was present in the gastric juice in 29 out of 53 (55%) pernicious anaemia patients studied by Rose (1970). In 11 (21%) the gastric-juice antibody was found only after it had been dissociated from intrinsic factor. The gastric-juice antibody often occurred in the absence of a demonstrable serum antibody, and of 27 patients without intrinsic-factor antibody in serum, such an antibody was present in gastric juice in 15. The purpose of this report is to describe further observations on these patients wherein the relationship between vitamin-B₁₂ absorption and the presence of intrinsic-factor antibody in serum or gastric juice was studied.

Patients and Methods

There were 29 patients with pernicious anaemia who were studied at St. Mary's Hospital, London. All had a megaloblastic anaemia due to vitamin-B₁₂ deficiency, histamine-fast or pentagastrin-fast achlorhydria, and impaired absorption of vitamin B₁₂ which was improved to a greater or less extent by additional intrinsic factor. The results in 35 patients with normal gastrointestinal function who were tested over the same period served as controls for vitamin-B₁₂ absorption.

Detection of intrinsic-factor antibody in serum was by the method of Ardeman and Chanarin (1963) and in gastric juice by the method of Rose and Chanarin (1969).

Vitamin-B₁₂ Absorption Tests.—Vitamin B₁₂ 1 µg labelled with ⁵⁷Co was mixed with a solution of 20 mg of dried hog intrinsic factor (Lederle WES 818) and given to the fasting patient. This was followed immediately by an injection of

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1,000 µg of cyanocobalamin and a 24-hour collection of urine. A plasma sample was taken 10 to 12 hours after the oral dose of vitamin B₁₂. Radioactivity was measured in both an aliquot of urine and the plasma sample. If the results by these two methods did not agree, suggesting incomplete urine collection, the result of the urine test was rejected and the test repeated.

Results

The results are shown in the Table. There was no significant difference in the urinary excretion of vitamin B₁₂ between the

Results of Vitamin-B₁₂ Absorption Tests (Urinary Excretion; Schilling Test). Percentage of Oral 1-µg Dose of ⁵⁷Co-Vitamin B₁₂ in Urine

	No.	Schilling Test	
		Mean	Range
Controls	35	19.2	11.2—32.0
Pernicious anaemia (with 20 mg hog intrinsic factor)	29	12.8	3.8—23.0
Intrinsic-factor antibody			
In serum			
+ —	6	19.3	15.8—23.0
— —	6	14.4	10.3—19.0
+ +	10	11.1	8.5—15.0
— +	7	8.4	3.8—13.4

control subjects, the pernicious anaemia group without demonstrable antibody, and the pernicious anaemia group with only serum antibody. On the other hand, the group with antibody in gastric juice excreted (and hence absorbed) significantly less vitamin B₁₂ than did those pernicious anaemia patients without antibody ($P=0.01$), and this was even more so when the group with antibody in both serum and gastric juice was considered.

Discussion

Though it has been accepted that under special circumstances antibody to intrinsic factor will interfere with vitamin-B₁₂ absorption, the data presented here indicate that in pernicious anaemia this is the rule rather than the exception. The most pronounced effect was found in the "best antibody formers"—that is, those who had antibody in both serum and gastric juice. The data also indicate that the presence of antibody is an important factor in producing the severe degree of malabsorption of vitamin B₁₂ that leads to severe vitamin-B₁₂ deficiency. Thus the appearance of an intrinsic-factor antibody is able to convert a moderate degree of vitamin-B₁₂ malabsorption that does not necessarily lead to vitamin-B₁₂ deficiency (as in many cases of atrophic gastritis) to the relatively severe malabsorption found in pernicious anaemia.

On the other hand, the data confirm previous observations that serum antibody alone is less significant and where the antibody is confined to the serum compartment may have no effect at all on vitamin-B₁₂ absorption (Rose, Chanarin, Doniach, Brostoff, and Ardeman, 1970).

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Factors Predisposing to Recurrent Haemorrhage after Acute Gastrointestinal Bleeding*

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Summary

A retrospective survey of 472 consecutive hospital admissions for acute upper gastrointestinal bleeding showed that patients with a large initial bleed are more likely to bleed again than those with a small initial bleed. The incidence of recurrent haemorrhage is also related to the interval since the last bleeding episode, so that patients showing no clinical evidence of haemorrhage for 48 hours are unlikely to bleed again in the near future. Patients admitted after a haematemesis have a higher incidence of recurrent haemorrhage than those admitted after melaena only. Aetiology has been confirmed as an additional important factor, the incidence being highest in those with oesophageal varices or a chronic gastric ulcer. Contrary to widespread belief, age does not appear to affect the incidence of recurrent haemorrhage, nor do other constitutional factors such as sex or the ABO blood group.

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Introduction

Recurrent haemorrhage after admission to hospital results in a twelvefold increase in medical mortality rate (Avery Jones, 1956) and is therefore generally regarded as the main indication for emergency surgery. Unfortunately, a policy of selective emergency surgery in these patients has failed to reduce the overall mortality rate significantly (Avery Jones, 1956; Schiller *et al.*, 1970). An improvement in mortality rate seems more likely to result from a policy of operating on patients before, rather than after, they rebleed, so that a method of recognizing patients at special risk of recurrent haemorrhage might have important therapeutic implications. Apart from the observation that patients with a chronic gastric ulcer are at an increased risk (Avery Jones, 1956), very little is known about factors predisposing to recurrent haemorrhage.

Methods

Careful records are kept in the gastroenterology department of all patients admitted to the Central Middlesex Hospital with acute gastrointestinal bleeding. Almost all these patients are admitted to one of the two gastroenterology wards. This system offers considerable advantages for retrospective analysis,