Intrinsic factor antibodies and intrinsic factor mediated vitamin B\textsubscript{12} absorption in pernicious anaemia

S. ARDEMAN AND I. CHANARIN

From the M.R.C. Experimental Haematology Research Unit and Department of Haematology, St. Mary's Hospital, London

EDITORIAL SYNOPSIS These studies indicate the possibility of an antibody to human intrinsic factor operating at cellular level in the small intestine in certain patients suffering from Addisonian pernicious anaemia.

There is considerable evidence to suggest that Addisonian pernicious anaemia is an autoimmune disease and that the transition from simple atrophic gastritis to pernicious anaemia is brought about by the development of an antibody to intrinsic factor. Briefly, intrinsic factor antibody is absent in patients with simple gastric atrophy but present in the majority of patients with Addisonian pernicious anaemia (Coghill, Doniach, Roitt, Mollin, and Williams, 1965; Ardeman, and Chanarin, 1963). The development of pernicious anaemia at a very young age (so-called ‘juvenile autoimmune group’) seems invariably to be associated with the presence of an intrinsic factor antibody (Doniach and Roitt, 1964). The association of pernicious anaemia and autoimmune thyroid disease (Doniach, Roitt, and Taylor, 1963) is such as to suggest that in both we are dealing with patients who have a genetically determined liability to develop an autoimmune type of disorder. On the other hand pernicious anaemia appearing in the first year of life with normal gastric histology is probably due to an inborn error of metabolism and is unrelated to the type presenting in later life.

The fact that intrinsic factor antibody is demonstrable in the serum of only 55\% of the patients with Addisonian pernicious anaemia suggests that in the remaining 45\%, either (1) the antibody is present at cellular level while absent from the serum, or, (2) in these the final failure of intrinsic factor mediated-vitamin B\textsubscript{12} absorption occurs by a mechanism not dependent on intrinsic factor antibody.

If an antibody against human intrinsic factor is present in all patients with pernicious anaemia, it seemed pertinent to enquire into the relative efficacy of hog intrinsic factor as opposed to human intrinsic factor in promoting vitamin B\textsubscript{12} absorption in pernicious anaemia. If antibodies to human intrinsic factor are present, human intrinsic factor might prove less efficacious than hog intrinsic factor in potentiating vitamin B\textsubscript{12} absorption; further if human intrinsic factor antibodies are present only in those patients in whom it can be demonstrated in the serum, then only these patients should show a poorer result in vitamin B\textsubscript{12} absorption tests with human intrinsic factor as compared to hog.

Despite the vast number of publications dealing with vitamin B\textsubscript{12} absorption we are aware of only two studies comparing the potentiating effect of human and hog intrinsic factor on vitamin B\textsubscript{12} absorption in the same pernicious anaemia patients. Schwartz, Lous, and Meulengracht (1958), using an 0.5 \textmu g. dose of oral vitamin B\textsubscript{12}, found that in three previously untreated patients the mean urinary excretion in the Schilling test was 22\% of the dose with hog intrinsic factor and 12\% with human intrinsic factor.

Abels (1959), using a 1.0 \textmu g. oral dose of vitamin B\textsubscript{12}, found that the mean urinary excretion in 10 patients was 18.1\% with 25 ml. human gastric juice and 17.9\% with a hog intrinsic factor preparation. The volume of gastric juice used would probably have provided an excess of human intrinsic factor but there is some doubt whether the hog intrinsic factor was present in excess. Reduction in the amount of hog intrinsic factor produced a fall in the urinary excretion of vitamin B\textsubscript{12}.

The purpose of the observations described in this paper was simply to compare the efficacy of a hog intrinsic factor concentrate with that of normal human gastric juice in promoting vitamin B\textsubscript{12} absorption in patients with Addisonian pernicious anaemia.
urinary excretion

Intrinsic

To

the

urinary

excretion

of

vitamin

B_{12}

was

less

effective

than

hog

intrinsic

factor

in

potentiating

vitamin

B_{12}

absorption

in

patients

with

pernicious

anaemia

(Table)

and

this

applied

equally

to

those

patients

with

demonstrable

intrinsic

factor

antibodies

and

to

those

without.

Human

gastric

juice

gave

a

higher

urinary

excretion

of

labelled

vitamin

B_{12}

in

only

three

of

the

19

cases

(Figure).

The

difference

between

the

hog

and

human

intrinsic

factor

results

in

the

pernicious

anaemia

group

was

statistically

significant

(\( p = 0.05 \)).

On

the

other

hand,

in

post-gastrectomy

subjects

a

slightly

higher

value

in

the

Schilling

test

was

obtained

when

the

test

was

carried

out

with

human

intrinsic

factor

as

opposed

to

a

hog

preparation.

COMMENT

The

use

of

a

heterologous

(hog)

intrinsic

factor

preparation

resulted

in

the

excretion

and

presumably

absorption

of

a

greater

amount

of

vitamin

B_{12}

than

was

the

case

when

the

homologous

intrinsic

factor

was

used.

The

probable

explanation

is

the

presence

of

an

antibody

to

human

intrinsic

factor

acting

at

small

gut

level.

There

is

some

degree

of

cross

reaction

between

the

human

intrinsic

factor

antibody

and

hog

intrinsic

factor

and

this

may

be

the

explan-
ation for the urinary excretion values in pernicious anaemia even with the hog preparation remaining below that found in control subjects. On the other hand this can hardly be the explanation for the lower urinary excretion in post-gastrectomy subjects. It is possible that after gastric resection intestinal malabsorption may be of some importance in producing a lower vitamin B12 absorption. Alternatively, Callender and Evans (1955) have shown in a different context that a large excess of intrinsic factor may improve vitamin B12 absorption. It is possible that a large excess of intrinsic factor may restore vitamin B12 absorption in pernicious anaemia to the values found in control subjects. Since the amount of intrinsic factor used in this study was sufficient to bind fully all the orally-administered vitamin B12, a large excess of intrinsic factor might function by protecting vitamin B12 intrinsic factor complex from the action of proteolytic enzymes.

There appeared to be no difference in the manner of vitamin B12 excretion in patients with demonstrable intrinsic factor antibodies and in those without. Thus if the reduced excretion with human intrinsic factor is determined by an antibody, then this antibody is present in both groups of patients. It is of some interest that when patients with Addisonian pernicious anaemia are treated with steroids an improvement in vitamin B12 absorption and return of intrinsic factor and hydrochloric acid to the gastric secretion occurs both in patients with a demonstrable intrinsic factor antibody and also in those without. Patients after gastrectomy, however, do not improve their vitamin B12 absorption with steroid therapy (Ardeman and Chanarin, 1965b).

We are indebted to Dr. Leon Ellenbogen, of Lederle Laboratories, for a supply of hog intrinsic factor concentrate.

SUMMARY

A comparison was made of the ability of hog intrinsic factor and human intrinsic factor given in excess to potentiate the absorption of 57Co-vitamin B12 in Addisonian pernicious anaemia. The mean urinary excretion of 57Co-vitamin B12 with the hog preparation was 14.2% and with human intrinsic factor 11.7%. The difference between the values was statistically significant (p = 0.05). This difference was not found in post-gastrectomy patients. The lower value with human intrinsic factor was attributed to the presence in cells of the villus of an antibody to human intrinsic factor.

REFERENCES


Intrinsic factor antibodies and intrinsic factor mediated vitamin B-12 absorption in pernicious anaemia.
S Ardeman and I Chanarin

*Gut* 1965 6: 436-438
doi: 10.1136/gut.6.5.436

Updated information and services can be found at:
http://gut.bmj.com/content/6/5/436.citation

**Email alerting service**
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Topic Collections**
Articles on similar topics can be found in the following collections:
Stomach and duodenum (1689)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/