since been shown to have impaired synthesis of metallothionein in culture fibroblasts. In our case, however, basal and metal induced metallothionein synthesis in skin fibroblasts was normal,2 indicating that heterogeneity exists among cases of primary, non-environmental, non-Wilsonian copper toxicosis.

S.P. HORSLEN
M.S. TANNER
University of Sheffield,
The Sheffield Children’s Hospital,
Sheffield S10 2TH

5 Hahn SH, Danks DM, Gahl WA. Normal metallothionein synthesis in fibroblasts obtained from children with Indian childhood cirrhosis or copper associated childhood cirrhosis. Biochemical and Molecular Medicine (in press).

Eradication rate of Helicobacter pylori

EDITOR,—The paper by Moshkowitz et al (Gut 1995; 36: 845–7) suggesting that the pretreatment 14C-urea breath test results are related to the outcome of triple therapy consisting of colloidal bismuth, metronidazole, and amoxicillin raises several points. Unfortunately, the authors did not include confounding variables such as compliance, metronidazole resistance testing, age, pretreatment with antibiotics and anti-secretory drugs, respectively, which may also have an important effect on the outcome of eradication therapy. Another weakness of this particular study is that the authors did not show the correlation between the urea breath test and histology, although biopsy specimens were taken for histological examination in all patients. On the basis of previously published comparison studies between breath test results and histology, the authors concluded that it is the density of H pylori that predicts the outcome of eradication therapy. We cannot agree with this conclusion.

Firstly, the breath test, as an indirect measure, may reflect the total gastric urease activity, however, urease activities may vary considerably between H pylori strains.1 Thus, in clinical practice the accurate prediction of the H pylori density by the urease breath tests will in all likelihood be the exception rather than the rule.

Several studies have shown that a significant correlation does exist between urea breath test and the histological density of H pylori infection and the severity of gastritis. But what does a significant correlation imply clinically? Because of the high sensitivity of statistical tests in correlation analyses, rather weak correlations may result in statistical significance. It is, however, the determination coefficient (squared correlation coefficient) that reflects the proportion of results that have been predicted properly when one of two correlated variables is known. For example, we have found highly significant correlations (p<0.0001) between the 13CO2 excess after intake of labelled urea and the histologically visible degree of H pylori colonisation (r=0.81), the degree of gastritis (r=0.72) and the activity of gastritis (r=0.69) as well.3 These correlations showed that the histopathological findings would have been predicted properly in 66%, 52%, and 48% of cases, respectively, which is of course clinically not very useful. It should also be mentioned that some of the studies quoted by Moshkowitz et al. were published only as abstracts, which do not permit the estimation of the clinical relevance of the correlations, because the correlation coefficients are not given.

Previous studies have suggested that the density of H pylori determines both the grade and the activity of gastritis.4 5 Recent studies have also shown that the severity of gastritis predicts the success of eradication therapy with triple therapy just as well.6 7 One study combining urease activity with metronidazole resistance and amoxicillin8 in the sense that a more severe gastritis is associated with a higher likelihood of eradication success. Grade and activity of gastritis reflect the specificity and sensitivity of the response of the host to the infection with H pylori. Although scientifically unconfirmed up to now, it seems to be plausible that comparable to other infectious diseases it is the immune response that facilitates eradication of H pylori whatever treatment is used. Provided the urea breath test used by Moshkowitz et al actually reflects the H pylori density and thus in turn the severity of gastritis, the finding of a higher eradication rate in patients with lower urea breath test values is in apparent contradiction to the studies quoted above.

In conclusion, despite a significant correlation the clinical usefulness of urea breath tests with respect to prediction of H pylori density and severity of gastritis remains yet unproved and such predictions should be used in clinical practice with caution. Also without exclusion of confounding variables by means of multiple logistic regression analysis it is actually impossible to identify a single factor independently governing the success of eradication therapy.

J. LABENZ
B. TILLENBURG
H. PEITZ
G. BÖRSCHE
Department of Internal Medicine and Gastroenterology, Elisabeth Hospital, and Molecular Medicine (in press).

Correspondence to Dr J. Labenz


Downloaded from http://gut.bmj.com/ on January 14, 2018 - Published by group.bmj.com
metronidazole in triple therapy does not improve the efficacy of treatment, but increases the risk of acquisition of metronidazole resistance.

Determination of bacterial density in the stomach may have some implications for the eradication of the organism. The urea breath tests, which can detect H pylori quantitatively, are not routinely available in most units at present. The biopsy dependent rapid urease tests, which are widely used and commercially available, have the potential to determine the bacterial density by measuring the urease activity quantitatively or semi-quantitatively—that is, the greater the number of organisms, the quicker the colour change because of the increased production of ammonia. The currently applied rapid urease tests, based on agar or liquid media, may need modifications for quantitative detection of H pylori in the stomach.

H X XIA
C T KEANE
Department of Clinical Microbiology,
CPL, St James's Hospital, Dublin 8, Ireland

CA O'MORAIN
Department of Gastroenterology,
Meath/Whitirea Hospitals, Dublin 8, Ireland


Reply

EDITOR.—We thank Dr Labenz and coworkers for their thoughtful comments on our study. They have raised basically two questions. The first one is whether a high gastric urease activity as measured by the 14C-urea breath test is indeed a factor in predicting the effectiveness of eradication with triple therapy? They suggest that other confounding variables might contribute to the strong correlation found. In addition, they wonder whether high urease activity found in the 14C-urea breath test repre- sents a high bacterial density in the stomach or more severe gastritis.

Concerning the potential confounding variables, we pointed out in the article that metronidazole resistance of H pylori seems to be infrequent in Israel (6% in a preliminary study). We have no data to suggest that compliance with therapy was different in the three patient groups. None of the patients in the study were pretreated with antibiotics or omepraizole in the four weeks before the test. The adverse effect of smoking as reported by Dr Labenz's group is controversial.1 2 Thus, we have no support for the assumption that these confounding variables might indeed be important factors. We therefore believe that urease activity as measured by 14C-urea breath test is an important independent variable in predicting the effectiveness of H pylori eradication with triple therapy. This is not necessarily true of future therapies, which may be more effective and therefore less dependent on the bacterial load. In addition, we are now studying the effect of some factors mentioned by Dr Labenz et al.

The other point is more theoretical. Dr Labenz et al question whether the correlation between the 14C-urea breath test values and density of H pylori colonisation as well as the degree of gastritis as reported by other investigators is clinically valid? Also, whether eradication might be more effective in more severe gastritis, which might reflect a stronger immune response? Our data do not permit answers to these theoretical considerations. As pointed out in our paper it is at present not known whether the higher urease activity results only from a higher bacterial load or also from different bacterial strains. This requires further investigation.

We thank Drs Xia, Keane and O’Morain for their valuable comments. We are happy that we agree with their conclusion that a higher bacterial load is of negative predictive value for the success of eradication of H pylori with triple therapy. They mentioned two important points: firstly, that resistance, particularly to metronidazole may develop during therapy. We agree, but would point out that the concurrent administration of bismuth salts, as inherent in the triple therapy, attenuates this effect. Secondly, they also suggest that a dose of metronidazole might have been too low, contributing to the overall low eradication rate. Here we have to point out a regrettable error. We gave 750 mg of metronidazole per day, that is, 250 mg three times daily. This was erroneously printed as 250 mg twice daily. Although 750 mg daily for two weeks is not a high dose, it has been shown to be effective and is less conducive to non-compliance.

Regarding their additional comment, we do not quite agree with their suggestion to use the rapid urease test (of gastric biopsy specimens) as a rough estimate of the gastric bacterial load. Unlike 14C-urea breath test, which reflects the overall gastric urease activity, the estimation based on a small biopsy sample is much more prone to sampling error.

M MOSHKOWITZ
F M KONIKOFF
T GILTAT
Department of Gastroenterology,
Tel-Aviv Medical Centre,
Ichilov Hospital,
6 Weizman Street,
64239 Tel-Aviv, Israel

NOTES

Sir Francis Avery Jones BSG Research Award 1996

Applications are invited by the Education Committee of the British Society of Gastroenterology who will recommend to Council the recipient of the 1996 Award. Applications (eighteen copies) should include:

1 A manuscript (2 A4 pages only) describing the work conducted.

2 A bibliography of relevant personal publications.

3 An outline of the proposed content of the lecture, including title.

4 A written statement confirming that all or a substantial part of the work has been personally conducted in the UK or Eire.

Entrants must be 40 years or less on 31 December 1996 but need not be a member of the BSG. The recipient will be required to deliver a 40 minute lecture at the Spring Meeting of the Society in 1996. Applications (eighteen copies) should be made to: The Honorary Secretary, BSG, 3 St Andrews Place, London NW1 4LB by 1 December 1995.

Hopkin's Endoscopy Prize 1996

Entries are invited by the Endoscopy Committee of the British Society of Gastroenterology for the BSG Spring Meeting in Brighton 1996.

The abstract should be confined to two sides of A4 paper but tables and references can be on additional pages. The entry can contain work previously presented/published (please give details).

A cover note should contain the address and post of the entrant.

The winner will give a 20 minute lecture (plus 10 minutes for questions).

The closing date for entries is 6 January 1996 and should be made to: Hopkin's Prize Entry, Dr D M Hellier, Secretary-Endoscopy Committee BSG, Department of Gastroenterology, Princess Margaret Hospital, Okus Road, Swindon SN1 4JU.
Eradication rate of Helicobacter pylori.

H Y Xia, C T Keane and C A O'Morain

_Gut_1995 37: 591-592
doi: 10.1136/gut.37.4.591-a

Updated information and services can be found at:
http://gut.bmj.com/content/37/4/591.2.citation

These include:

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.

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/