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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.[8] The currently applied rapid urease tests, based on agar or liquid media, may need modifications for quantitative detection of *H pylori* in the stomach.

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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 ^{14}C-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 ^{14}C-urea breath test represents 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 omeprazole 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 ^{14}C-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 ^{14}C-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 they agree with our 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 our 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 thrice 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.[3]

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 ^{14}C-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.

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NOTES

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