Correspondence

Interaction of Campylobacter pylori . . .

Sir,—We read with interest the paper by Bernatowska et al (Gut 1989; 30: 906–11). Their observations that Campylobacter pylori will activate the classical pathway of complement directly and can be phagocytosed by neutrophils in vitro may well be of considerable importance. The role of complement in vivo at the gastric mucosal surface must, however, be questioned.

It has been known for many years that ammonia can inactivate complement. Host defence mechanisms are known to be compromised in the kidney because of the inactivation of complement.1 These early studies of Beeson and Rowley suggested that ammonia production by renal glutaminase could inactivate the fourth component of complement. Ammonia production from urease positive bacteria colonising the urea rich environment of the kidney has also been proposed as a source of anti-complementary activity.2 Campylobacter pylori is known to have potent urease activity3 and in the presence of urea it is highly likely that viable organisms will produce concentrated ammonium ions in close proximity to gastric epithelial cells.

The study of Bernatowska et al was carried out with heat killed C pylori (60°C for one hour), a process which will virtually abolish the marked urease activity of the bacterium.4 C pylori has been shown to generate considerable quantities of ammonia from urea in vitro5 and in vivo the concentration of ammonia in gastric juice correlates with the presence or absence of C pylori.6 Local ammonia production by these bacteria at the gastric luminal surface might, therefore, comprise mucosal defences by inactivation of complement in a similar manner to that proposed in the kidney.

It would be of interest therefore to know whether the results of Bernatowska et al would have been different had the experiments been undertaken with live C pylori in the presence of urea. The ammonia produced under such conditions might well be expected to modify the activation of complement by C pylori and the subsequent neutrophil phagocytosis.

J E CRABTREE, T M SHALLCROSS, AND R V HEATLEY
Department of Medicine,
St James’s Hospital,
Leeds LS9 7TF

References


Reply

Sir,—Dr Crabtree and colleagues raise the interesting point that ammonia produced by live Campylobacter pylori might inactivate complement in vivo. Our studies on complement activation were performed with organisms scraped from blood agar plates and suspended in phosphate buffered saline, and then stored at −70°C until used. Only the organisms used for the ELISA antibody assays were heat killed. It is unclear, however, whether the organisms used in the complement studies were metabolically active and able to produce ammonia. This would need further investigation, and it might be difficult to design a system of in vitro complement activation with actively metabolising organisms. In order to assess the in vivo relevance of our findings, immunofluorescent studies to identify C5a in gastric biopsies from patients with gastritis and C pylori infection may be rewarding.

A D B WEBSTER

CRC,
Immunodeficiency Referral Laboratory,
Watford Road,
Harrow,
Middx HA1 3UJ

Acid perfusion in the assessment of non-cardiac chest pain

Sir,—We would like both to point out some anomalies in the paper on acid perfusion in the assessment of non-cardiac chest pain from Hewson et al7 and to express doubts about their conclusion that the acid perfusion test (APT) may have been rendered obsolete by prolonged ambulatory intraoesophageal pH monitoring.

Firstly, they report that reproduction of chest pain (not heartburn) by APT occurred in 16/71 (22.5%) of their patients, a substantially different figure from that of 7% reported in a recent large series from the same laboratory.8 The figure of 22.5% is similar to the results we9 and Janssens and colleagues10 have reported (35% and 27% respectively). It is difficult to understand why in Hewson et al's study a symptom
index of >25% is chosen with regard to prolonged pH monitoring, when previous reports from the same group have indicated that a symptom index of >75% should be taken as indicating that chest pain is related to acid gastro-oesophageal reflux (GOR). This last point is crucial, as their conclusions depend largely on the finding that the symptom index identifies more patients with an acid sensitive oesophagus than acid perfusion tests.

Secondly, although Hewson et al briefly address the question, they seem to confuse the identification of an acid sensitive oesophagus by the APT with the diagnosis of GOR, when of course the APT does not detect GOR. They appear not to attach any significance to a positive APT in patients who do not have pathological GOR during pH monitoring.

We have previously reported that some patients develop chest pain in association with motility changes during oesophageal acid perfusion, but do not have abnormal GOR during subsequent prolonged pH monitoring. Vantrappen and colleagues report similar findings in 33 patients with non-cardiac chest pain, observing that chest pain could be related to more than one mechanism (one or more of the following: reflux without motor disorders, motor disorders without reflux, motor disorders without reflux but with a positive APT and acid reflux without motility disorders but with a positive edrophonium test). We would support their contention from our own studies. In this context, Vantrappen’s group propose the concept of the ‘irritable oesophagus’.

To show the value of APT, we wish to present further results in 45 patients with non-cardiac chest pain who had both APT and prolonged oesophageal pH monitoring with calculation of the symptom index (Table). A positive APT required reproduction of the patient’s pain (not heartburn).

A symptom index of >50% has been taken to indicate acid mediated chest pain. Our previous experience has been that 8/35 (23%) of chest pain patients with abnormal amounts of acid GOR would have been regarded as having negative symptom indices (and therefore pain not related to acid reflux) had a ‘cut off’ of 75% been used (unpublished data).

Two points emerge from the Table: firstly, acid perfusion identified acid related chest pain in three patients with abnormal amounts of GOR who either had a low symptom index or no symptoms during prolonged pH monitoring. Secondly, acid perfusion identified six patients with an acid sensitive oesophagus but normal amounts of GOR. Two of these also had a symptom index of >50%. Thus APT identified the oesophagus as the source of chest pain in 7 (54% of all positive APT) all of whom were not so identified by prolonged pH monitoring.

In conclusion, we are not persuaded that the acid perfusion test has been superceded by 24 hour pH monitoring for patients presenting with non-cardiac chest pain. Acid perfusion does not identify patients as refluxers, but as individuals with an acid sensitive oesophagus. If acid sensitivity is identified, 24 hour pH monitoring may then by required to establish whether it is related to GOR.

**Correspondence**

J S DE CAESTECKER* AND R C HEADING†

*Department of Medicine II, St George’s Hospital Medical School, Cranmer Terrace, London SW17 0RE

†Department of Medicine, Royal Infirmary, Edinburgh EH3 9YW

**References**


5. Ward BW, Wu WC, Richter JE, Lui KW, Castell DO. Ambulatory 24-hour esophageal pH monitoring: tech-
Correspondence


Reply
Sir,—The letter by de Caestecker and Heading raised several points worthy of comment:
(1) As performed in our two respective laboratories, the acid perfusion tests (APT) involves the infusion of 70–146 ml 0.1 N HCl over 10–15 minutes. What similarity does this test have with natural gastrooesophageal reflux disease (GOR) and our patient’s symptoms? In the latter disease, patients are usually refluxing volumes ranging from 2–50 ml and the contents contain pepsin, trypsin, and bile salts as well as acid. While the APT only assesses acid sensitivity, prolonged intraoesophageal pH monitoring with symptom correlation is, in fact, an ‘endogenous’ APT test which allows us assessment of the relationship between multiple spontaneous chest pain episodes and the ‘activated’ gastric contents. As we have previously shown, the APT is an excellent test for identifying acid sensitivity in patients with oesophagitis. The study is really superfluous in these individuals however, as they have already undergone endoscopy. In patients with non-cardiac chest pain who usually have normal endoscopic examinations, we want our screening tests to have relatively good sensitivity as well as specificity. More importantly, we want our screening tests to identify patients in whom an appropriate therapeutic intervention that it, aggressive acid suppression – will improve or relieve their symptoms. Unfortunately, unlike our British colleagues, our retrospective and more recently prospective experience suggests the APT test has some severe shortcomings.
(2) The appropriate definition of a positive symptom index is unknown at this time. In our original report (Am J Gastroenterol 1988; 83: 358–361), a symptom index of >75% was considered positive for chest pain and heartburn. Closer examination of these data, however, show that all subsets with ratios>25% had a higher prevalence of abnormal GOR (Figure 1 and 2 in that reference). We have recently treated and followed 20 patients whose symptom index was >25%. All patients received vigorous H2 blocker therapy (famotidine 40 mg tid or ranitidine 300 mg bid). Fifteen of 20 patients improved or had complete resolution of their symptoms (nine had abnormal GOR, six normal GOR). We believe this experience is additional support for our criteria of a symptom index >25% defining patients who most likely will respond to vigorous acid suppression. No percentage, however, has 100% positive predictive value. In the future, studies with more aggressive acid suppression – that is omeprazole – may better define an appropriate symptom index, although again it is doubtful that any value will be a perfect predictor of medical response.
(3) Our initial study was a retrospective review and frankly the results were somewhat surprising. Therefore, we undertook a prospective study before ‘closing the door’ on the APT. The preliminary results for our first 75 patients are detailed in the Table. A positive APT required reproduction of the patient’s pain, not just heartburn. These results were compared with the findings of a positive symptom index for chest pain defined as greater than 25% for the reasons previously stated.

Table Relationship between acid perfusion test (APT) and positive symptom index (SI>25%) on prolonged intraoesophageal pH monitoring

<table>
<thead>
<tr>
<th>pH test (SI&gt;25%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>APT</td>
</tr>
<tr>
<td>+</td>
</tr>
<tr>
<td>-</td>
</tr>
</tbody>
</table>

Sensitivity: 14/44 (32%) + Predictive value: 14/15 (93%)
Specificity: 30/31 (97%) – Predictive value: 30/60 (50%)

Our prospective study does suggest good specificity and positive predictive value for the APT. If you substitute the APT for prolonged intraesophageal pH monitoring, however, you will miss over two-thirds of your acid sensitive patients. In this prospective study, it also was interesting to note that the symptom index positive percentage was not significantly different for the positive APT patients (60.5% (6.1) (SE)) versus those with a negative APT (52.8% (4.8)). Therefore, the degree of positive symptoms correlation does not seem to be a factor in predicting the APT test results.

In conclusion, the APT can be used as a screening test in patients with non-cardiac chest pain, particularly if prolonged pH monitoring is not available. If the test is positive, the correlation with acid related chest pain during prolonged pH monitoring is excellent. If the test is negative, which is usually the case, it tells you nothing and these patients still need either prolonged intraoesophageal pH monitoring or an aggressive trial of H2 blocker therapy.

Is the APT test obsolete? Maybe not. Is it ‘a good’ screening test? Our experience would suggest no if you desire a reasonably sensitive test. As suggested
Acid perfusion in the assessment of non-cardiac chest pain.

J S de Caestecker and R C Heading

*Gut* 1989 30: 1795-1798
doi: 10.1136/gut.30.12.1795-b

Updated information and services can be found at:
http://gut.bmj.com/content/30/12/1795.3.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/