

LETTERS TO THE EDITOR

Bacterial adhesion and *Helicobacter pylori*

SIR,—We read with great interest the important paper by Dr Hessey and colleagues (*Gut* 1990; 31: 134–8). Our ultrastructural studies^{1,2} also confirmed the close relation between the direct adhesion of *Helicobacter pylori* to gastric epithelium cells and epithelial degeneration, and we agree that this relation support a pathogenetic

role of *H pylori* in chronic gastritis. We suspect, however, that the three categories of adhesion site observed by the authors may be conditioned by technical factors. When a bacterium is cut longitudinally all three of the described adhesive categories can be recognised (Fig 1): how the bacterial surface is transversally cut may affect how bacterium is classified.

An interesting question is whether *H pylori* adhere before or after epithelial degeneration occurs, and we agree with Hessey *et al* that bacterial adhesion may play a part in cell degeneration. Our ultrastructural figures show the tendency of *H pylori* to adhere to the cell surface already when primarily colonising the gastric epithelium: the large majority of bacteria (seen within the mucus layer) resting

on or are adherent to the short and irregular microvilli of an intact gastric epithelium, rather than suspended in mucus layer (Fig 2). Successively, possibly through the production of mucinase and cytotoxic activity,^{3,4} *H pylori* may induce mucin depletion and microvillar and cellular damage. Damaged areas might be more susceptible to the acid attack. We also noted a decrease in the number of bacteria and in the extension of colonised areas when mucin depletion and cellular degeneration are present, as if the bacterial survival would be linked to a defined tissue background and the close adhesion to the epithelial wall would be the only alternative way of life.

Finally, our histological preliminary data seem to indicate that the type of chronic gastritis (superficial or atrophic chronic gastritis) and the presence of histological activity do not influence the modes of contact between *H pylori* and gastric epithelium; the only relevant feature seems to be whether epithelial degeneration is present or not.

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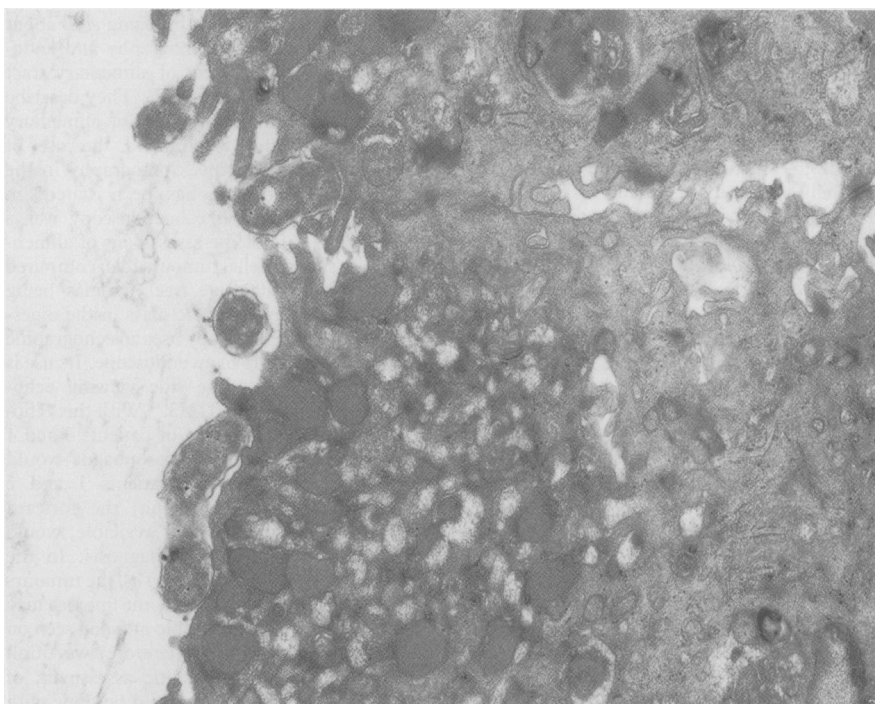


Figure 1: Gastric antral biopsy. Ultra thin section uranyl acetate-lead citrate stained. A longitudinally cut *Helicobacter*-like organism is recognisable. Original magnification $\times 15\,000$.

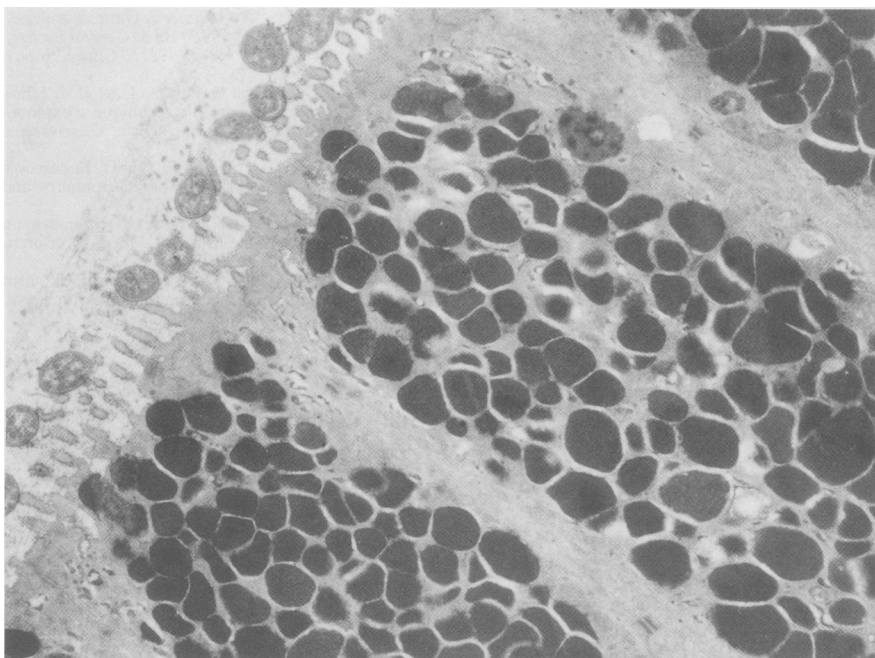


Figure 2: Gastric antral biopsy. Ultra thin section uranyl acetate-lead citrate stained. A large majority of *Helicobacter*-like organisms are resting on or are adherent to the microvillar surface of an intact epithelium. Original magnification $\times 12\,000$.

- 1 Caselli M, Figura N, Trevisani L, *et al*. Patterns of physical modes of contact between *Campylobacter pylori* and gastric epithelium: implications about the bacterial pathogenicity. *Am J Gastroenterol* 1989; 84: 511–3.
- 2 Caselli M, Bovolenta MR, Alcott A, *et al*. Epithelial morphology of duodenal bulb and *Campylobacter*-like organisms. *J Submicrosc Cytol Pathol* 1988; 20: 237–42.
- 3 Slomiany BL, Bliski J, Sarosick J, *et al*. *Campylobacter pyloridis* degrades mucin and undermines gastric mucosa integrity. *Biochem Biophys Res Commun* 1987; 144: 307–14.
- 4 Figura N, Guglicmetti P, Rossolini A, *et al*. Cytotoxin production by *Campylobacter pylori* strains isolated from patients with peptic ulcers and from patients with chronic gastritis only. *J Clin Microbiol* 1989; 27: 225–6.
- 5 Leunk RD, Johnson PT, David BC, *et al*. Cytotoxic activity in broth-culture filtrates of *Campylobacter pylori*. *J Med Microbiol* 1988; 26: 93–9.

Reply

SIR,—Drs Caselli and Alvisi suggest that the three forms of adhesion we describe can be shown by the same organism and that their distinction is artificial. While it is true that an organism could in one plane of section be categorised as abutting and in another be seen to indent the plasma membrane, we feel confident that only a minority of organisms exhibit attachment by fully-formed pedestals. Hitherto, this latter feature has received much attention in the literature and our purpose in categorising the attachment sites was to emphasise the relative infrequency of adhesion pedestal formation compared to the number of organisms in intimate contact with the plasma membrane. Nevertheless, we did acknowledge that these various appearances were likely to be different stages in the process of adhesion which is why they were amalgamated for the purposes of analysis.

A further point at issue is the sequence of events leading to bacterial adhesion. Drs Caselli and Alvisi describe *H pylori* first coming into contact with the microvillus border (primary colonisation?) where cytotoxin production and mucolytic activity cause cellular damage and disrupt the mucus barrier rendering the area more susceptible to acid attack. They have argued elsewhere that the bacteria then attach to the epithelium as a survival mechanism and that if it were not for bacterial adherence 'after degradation of the protective mucus layer, *C pylori* would be rapidly washed out from the stomach.'¹

It was not our intention to imply that cytopathic events only start with bacterial adhesion. It is self evident that the loss of microvilli which precedes and facilitates close attachment must be a manifestation of cell injury. It seems, however, that cell adhesion is required for more severe cytopathic effects and possibly the induction of an immune response. This could explain the finding of *H pylori* in the mucus layer above apparently normal corpus mucosa in some cases of antral gastritis. We do not agree that bacterial adherence is likely to be a late event after epithelial injury sufficient to cause mucin depletion and cellular degeneration. On the contrary, we were surprised at the lack of degeneration seen ultrastructurally in surface cells bearing adherent organisms. Furthermore, the accumulation of actin filaments seen at bacterial attachment sites and most pronounced beneath adhesion pedestals¹ presupposes a degree of cytoplasmic integrity and metabolic homeostasis incompatible with advanced degeneration.

Finally, with regard to bacterial survival, there would be little biological advantage to be gained from a mechanism which involved attachment to degenerate cells soon to be exfoliated into the gastric lumen.

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- 1 Caselli M, Figura N, Trevisani L, et al. Patterns of physical modes of contact between *Campylobacter pylori* and gastric epithelium: implications about the bacterial pathogenicity. *Am J Gastroenterol* 1989; 84: 511-3.
- 2 Smoot DT, Mobley HLT, Gilliam T, Phelps P, Resau JH. Pedestal formation of *Helicobacter (Campylobacter) pylori* with gastric epithelial cells *in vitro* may require actin polymerization. *Gastroenterology* (in press).

An old student's memories

SIR,—In reference to the birthday tribute to Sir Francis Avery Jones (*Gut* 1990; 31: 489-93) I would like to pay tribute to my chief Sir Francis Avery Jones, father of modern British gastroenterology.

I was introduced to him on my first arriving in Britain as a British Council postgraduate scholar in 1965, by Professor Hugh Morgan to whom I was medical registrar in Khartoum University Hospital. He was surrounded by his distinguished collaborators Kellock, Rowland, Richard Doll, Edward Shiner, Lennard-Jones, Misiewicz, and Langman. I joined him as clinical assistant, and then attended the second gastroenterology course conducted by the British Postgraduate Medical Federation in various London teaching hospitals, including the Central Middlesex, for 12 postgraduates from a dozen different countries, Sudan being represented for the first time. He introduced me to Sidney Truelove in Oxford, with whom I worked as honorary registrar to study aspects of ulcerative colitis, Crohn's disease, and the irritable bowel syndrome; to Sir Christopher Booth at Hammersmith for absorption and metabolic studies; and to Dame Sheila Sherlock for experience in hepatology.

His working day was always full and his tolerance and abilities in late middle age excelled ours in the prime of youth. The rounds, teaching sessions, and clinical meetings were so instructive that no one ever felt monotony or boredom. His approach was so modest, with interest and excitement in everyone's contribution. He thus created in all the desire and

curiosity for more teaching and more learning. I concur with Lennard-Jones's statement: 'He poked, rather than palpated, the abdomen in a rapid and seemingly casual manner but he always knew what he was looking for. His skill was born of the listening ear, immense experience and uncanny intuition.'

When we finished late at Central Middlesex he would drop us at our residence in his Rolls Royce. His frequent unforgettable cosmopolitan gatherings at 44 Cleveland Square for postgraduates, staff, and frequent continental and overseas visitors were happy occasions and created everlasting friendships between people from all parts of the world. It was an opportunity not to be missed including the personal experience which you never see, hear, or read about anywhere. One of the dictums he taught me was: There are two types of duodenal ulcers, the bleeding ulcer and the painful ulcer; the bleeding is painless and the painful does not bleed; if they die of their ulcers it is through exsanguination in the former and perforation in the latter.

You will find graduates of the Avery Jones school in every corner of the world; they naturally differ in nationality, skin colour, habits, religion, and mother tongue, but they are unanimously similar in one thing, and that is their affection for Avery.

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Obscure anaemia and hepatic dysfunction in Castleman's disease

SIR,—The fascinating case of Castleman's disease described by Featherstone *et al* (*Gut* 1990; 31: 834-7) bears a striking similarity to that of a young woman under our care.

She had a long history of vague ill health from the age of 20. Clinical examination was normal but she was found to have moderate anaemia (haemoglobin 8-10 g/dl), hyperglobulinaemia (IgG 55.8 g/l, IgA 6.2 g/l, IgM 3.6 g/l) and a raised erythrocyte sedimentation rate (100-130 mm in the 1st h). Bone marrow examination was essentially normal and a haematological diagnosis of anaemia of chronic disease was made. The patient continued to complain of malaise and the abnormal laboratory tests persisted.

Ten years after the onset of her symptoms she developed generalised pruritus and liver function tests were abnormal (alkaline phosphatase 912 U/l, γ glutamyl transferase 122 U/l, alanine aminotransferase 25 U/l, bilirubin 6 mmol/l). Liver biopsy specimen showed mild non-specific inflammatory changes. At this stage a Kveim test was positive and a course of prednisolone was given. There was no response by clinical or laboratory criteria and steroid treatment was withdrawn.

Three years later, 13 years after the initial presentation, the patient developed menorrhagia. An ultrasound scan of the pelvis showed a large paraovarian mass. At laparotomy a 10 cm retroperitoneal tumour with enlarged para-aortic and parailiac lymph nodes was resected. After the operation the patient lost all symptoms and health returned to normal. The anaemia, hyperglobulinaemia, and abnormal liver function tests resolved, although three years later the erythrocyte sedimentation rate remains slightly raised at 23-35 mm in the first hour. Histology of the resected tissue showed angiofollicular lymph node hyperplasia of the plasma cell type.

In our patient, as in the patient described by Featherstone *et al*, there was a long history of vague ill health and unexplained anaemia, hyperglobulinaemia, and abnormal liver function tests. The diagnostic process was protracted, which is unfortunate in view of the gratifying results of surgical excision. This diagnosis should be considered earlier in a young patient who presents with these features.

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Role of computed tomography, endoscopy, and echoendoscopy in the management of alimentary tract lipomas

SIR,—We read the paper by Kang *et al* about the role of computed tomography and endoscopy in the management of alimentary tract lipomas (*Gut* 1990; 31: 550-3). They describe the management of four cases of alimentary tract lipomas and recommend the use of endoscopy and computed tomography in the diagnosis. Recently it has been stated, in different studies, that echoendoscopy was a better procedure in the assessment of alimentary tract subepithelial tumours than computed tomography,¹⁻³ digestive tract lipomas being visualised as a hyperechoic mass in the digestive tract.¹ Echoendoscopy uses an echographic transducer at the tip of an endoscope. Its use is increasing. We use the side viewing echoendoscope, Olympus EUM3.^{1,4} With this echoendoscope the exploration of patients 3 and 4 (lipomas of the sigmoid and oesophagus) would have been possible. For patients 1 and 2 (lipomas of colon and ileum) the forward viewing echocoloscope, now available, would also have given a correct diagnosis. In the patients reported on by Kang *et al*, the tumours were over 3 cm in diameter. Some lipomas may be smaller and hardly capable of being seen on computed tomography. Therefore, we think that today the pretherapeutic assessment of alimentary tract lipomas should be done with endoscopy and echoendoscopy.

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- 1 Amouyal P, Amouyal G, Palazzo L, et al. L'échoendoscopie: une nouvelle technique d'exploration des tumeurs sous épithéliales. *Gastroenterol Clin Biol* 1990; 14: 8-14.
- 2 Silva SH, Kouzot T, Ogino Y, Sato H. Endoscopic ultrasonography of oesophageal tumours and compressions. *JCU* 1988; 16: 149-7.
- 3 Tio TL, Tytgat, GNJ. *Atlas of transintestinal ultrasonography*. Aalsmeer: Mur-Kosverloren, 1986.
- 4 Palazzo L, Roseau G, Gayet B, Amouyal P, Ponsot P, Paolaggi JA. L'endoscopie digestive. *Presse Méd* 1989; 18: 1748-52.

Reply

SIR,—We thank Drs Roseau and Paolaggi for their comments. We have no personal experience of echoendoscopy but agree that it should be superior to computed tomography in the evaluation of submucosal lesions. This modality, however, unlike computed tomography, is as yet of limited availability. Our comments on computed tomography relate to large lesions since those smaller than 1-2 cm may not be able to be visualised.

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