

quence of impaired uterine or ovarian development during the mother's own fetal life.<sup>34</sup>

One observational study cannot form the basis for changing dietary recommendations to pregnant women. The differing relations of nutrient intakes in early and late pregnancy to placental and fetal growth need replication in other studies. Our findings, however, do parallel those of experimental studies in sheep in which high nutrient intakes in early pregnancy have been shown to suppress placental and fetal growth.

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## Omeprazole as a risk factor for campylobacter gastroenteritis: case-control study

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Gastric acid protects against enteric infections,<sup>1</sup> and patients who have had gastric surgery or are taking H<sub>2</sub> antagonists are more susceptible to salmonella infection.<sup>2,3</sup> Antibiotic treatment also increases the risk of infection.<sup>3</sup> It is not known whether these factors are also associated with campylobacter infection, for which statutory notifications now exceed those for salmonella.<sup>4</sup> We conducted a case-control study to assess whether gastric antisecretory drugs, antibiotics, and abdominal surgery are associated with campylobacter infection.

### Patients, methods, and results

Between January 1992 and August 1994, 243 notified cases of campylobacter infection, confirmed by faecal culture, were identified in people aged 45 and

over in two of the local district councils within Nottingham Health Authority. Thirty two cases were excluded (non-resident (four), general practitioner declined (19), patient died and notes unobtainable (six), and notes unobtainable at general practice (three)), leaving 211 (123 women). The minimum age was 45 because people over this age have higher rates of prescribing by general practitioners. Controls were identified as the next two patients matched for sex and age within two years in the practice computerised records. No controls were excluded.

Data on previous surgical operations; prescriptions for H<sub>2</sub> antagonists, proton pump inhibitors, antibiotics, hydroxocobalamin, and corticosteroids; and regular prescriptions and other drugs used before infection were extracted from the general practice records. Data were analysed by conditional logistic regression using the EGRET package with the magnitude of associations measured by odds ratios. The study had 80% power to detect a 2.5-fold risk, given that 4% of the general population was exposed.

Omeprazole treatment in the month before infection was associated with a 10-fold increased risk of campylobacter infection (table 1). This was independently significant only for current use. The association with H<sub>2</sub> antagonists was not significant after omeprazole use was controlled for. Antibiotic treatment in the two to

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**Table 1—Odds ratios for associations with campylobacter infection**

Exposure	Cases (n=211)	Controls (n=422)	Odds ratio (95% confidence interval)	
			Unadjusted	Adjusted
Omeprazole:				
In month before infection	10	2	10.0 (2.2 to 46)	11.7 (2.5 to 54)
2-12 Months before infection	7	4	3.5 (1.0 to 12)	0.7 (0.1 to 4.4)
Ever used	13	5	5.2 (1.9 to 15)	5.8 (2.0 to 17)
(Excluding current users)	3	3	2.0 (0.4 to 10)	2.1 (0.4 to 11)
H <sub>2</sub> receptor antagonists:				
In month before infection	12	14	1.8 (0.8 to 3.9)	1.8 (0.8 to 4.4)
2-12 Months before infection	22	25	1.8 (1.0 to 3.3)	1.1 (0.4 to 2.9)
Ever used	35	44	1.7 (1.1 to 2.7)	1.2 (0.7 to 2.1)
(Excluding current users)	23	30	1.6 (0.9 to 2.7)	0.9 (0.4 to 2.1)
Antibiotics:				
In month before infection	11	24	0.9 (0.4 to 1.9)	0.6 (0.3 to 1.3)
2-12 Months before infection	74	95	2.0 (1.3 to 2.9)	2.1 (1.4 to 3.0)
Previous gastric surgery	1	9	0.2 (0 to 1.7)	0.2 (0 to 1.6)
Hydroxocobalamin treatment	2	3	1.3 (0.2 to 10)	1.1 (0.2 to 6.60)

\*Controlled for use of omeprazole, antibiotics, and other drugs.

12 months before infection was associated with a relative risk of 2. No associations were seen with previous gastric or colonic surgery, pernicious anaemia, corticosteroids, use of other drugs, or the number of regular prescriptions. Analyses of subgroups by age (over 65, under 65) and sex showed the same associations.

**Comment**

Our results show that use of omeprazole predisposes to clinical campylobacter infection. The finding that current users but not former users of omeprazole were at increased risk suggests that the relation is causal. Omeprazole probably increases the risk or severity of infection by reducing the gastric killing of ingested organisms. Some cases of diarrhoea with omeprazole may be infective and should be investigated by faecal culture.

No relation was seen with H<sub>2</sub> antagonists despite the power of the study to detect a relative risk of 2.5 for H<sub>2</sub> antagonist use in the month before infection. H<sub>2</sub> antagonists reduce gastric acidity less than proton pump inhibitors, which could leave sufficient acid to reduce the ingested dose of campylobacter organisms.

The increased acid suppression with omeprazole allows more organisms to survive, so increasing the risk of clinical infection. Campylobacters are more acid sensitive than are salmonella.<sup>4</sup> Severity of salmonella infection is related to size of infecting dose,<sup>5</sup> and the same may apply to campylobacter. The greater acid sensitivity of campylobacter may also explain the lack of association seen with previous gastric surgery, which produces relatively modest reductions in acid secretion. Our results also suggest that antibiotics increase the risk of campylobacter infections, as with salmonella<sup>3</sup>; use of antibiotics may predispose to infection by altering bowel flora.

The absence of an association with hydroxocobalamin, which was used as a proxy for pernicious anaemia, and similar findings for salmonella,<sup>3</sup> is surprising and suggests that other factors are important. Many of our patients had recently started taking omeprazole; temporary reduction in acid may be important, and different factors may operate in long term acid reduction, such as changes in bacterial flora, which protect against campylobacter and salmonella infection.

In conclusion, proton pump inhibitors lead to a significant increased risk of campylobacter infections in people aged 45 or over, an effect not seen with H<sub>2</sub> antagonists or previous gastric surgery. This can be explained by differences in acid suppression and the pH sensitivity of campylobacter.

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**A PATIENT WHO CHANGED MY PRACTICE**

**Torture**

She was just an ordinary woman with an ordinary problem. It was the Sunday evening of a normal weekend on call. I was an average first year senior house officer in general medicine. Yet the conversation that I had with her in the middle of the ward during the lull which followed the storm of the previous 36 hours was to change my practice, my career, my future.

She had an extraordinary tale, told rather haltingly in her slightly foreign accent. It was a tale of torture years before at the hands of a foreign organisation. As she spoke, I could picture the anguish, empathise with all she must have felt, share her relief to have survived this far.

She had been taken prisoner and shut in a room with her tormenters. Separated from her family, she was to be allowed no rest, but every so often she was encouraged to think that she might soon be able to catch some sleep. There would be a lull in the proceedings followed by a period of sheer terror. There was no food and little to drink. Everything would build up to a frenzy of interrogation, then stop abruptly. Just as she was begin-

ning to relax a petty irritation of minor importance would interrupt her. She was exhausted and short tempered, but shouting at her captors only made them more determined to keep her awake. And always there was the promise of sleep, which was never quite fulfilled. For two whole days she had endured this—two whole days.

Her description perfectly fitted my weekend so far. There had been the mundane bloods round, the usual admissions, the cardiac arrests, the worry about the bed state. I had not slept at all the previous night and was not likely to fare much better that day, but I had briefly reached the haven of my room several times. The canteen was closed whenever I had the time to eat; the food dispensing machine was empty.

Talking with my patient had shown me my life. When my contract finished so did I. Five years on I am a housewife and mother and have never once regretted my decision to leave medicine. But I still feel resentment about a system which could encourage such torture in its own land yet condemns barbarism abroad.—ALISON MARTIN is now a housewife in Essex