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Letters to the editor

Eradication of *Helicobacter pylori* decreases mucosal alterations linked to gastric carcinogenesis in Mongolian gerbils

To the Editor: Helicobacter pylori (*H. pylori*) infection increases the risk of gastric carcinogenesis, and Mongolian gerbils have served as useful models for investigation of *H. pylori*-induced gastric disorders, including gastric cancer.[1–3] It was shown recently that *H. pylori* eradication decreased *N*-methyl-*N*-nitrosourea (MNU)-induced gastric carcinogenesis in gerbils.[4] However, no pathological investigation on the relationship between *H. pylori* eradication and gastric carcinogenicity has been conducted in this model. Therefore, we evaluated the effect of *H. pylori* eradication on gastric mucosal changes in relation to carcinogenicity.

Twelve Mongolian gerbils (specific pathogen-free, 7 weeks old, male; Seac Yoshitomi, Fukuoka, Japan) were inoculated with 8×10^8 colony-forming-units of *H. pylori* (ATCC43504; American Type Culture Collection, Rockville, MD, USA). Half were treated with a course of amoxycillin (1 mg/kg) plus omeprazole (10 mg/kg) 24 weeks after the inoculation; the drugs were suspended in 0.5% hydroxypropylmethylcellulose and administered i.g. twice daily for 10 days. Six gerbils not inoculated with *H. pylori* served as controls.

Forty weeks after the inoculation, all the gerbils were killed. Thirty minutes before being killed, the gerbils were given 5′-bromo-2′-deoxyuridine (BrdU) intraperitoneally (200 mg/kg), and blood samples were obtained to measure the titer of anti-*H. pylori* IgG antibody using an enzyme-linked immunosorbent assay. Tissue sections of the excised stomachs were stained with hematoxylin and eosin (H&E) or Alcian blue (pH 2.5)–periodic acid-Schiff. The degree of inflammation was graded according to the Updated Sydney System, as described previously.[2]

One gerbil from the untreated group died at 32 weeks after *H. pylori* inoculation. All the gerbils in the *H. pylori*-inoculated groups were seropositive for *H. pylori*, and the antibody titer in the treated group was significantly lower than that in the untreated group at the time of death (Table 1). The development of gastric polyps (defined as 2 mm or more elevated mucosal lesion) and the grades of inflammatory cell infiltration in the gastric mucosa were significantly lower in the treated than the untreated group (Fig. 1, Table 1). There were fewer intestinal metaplastic foveolae in the treated than the untreated group, but this finding was not significant. None of the control gerbils showed any pathological changes of the gastric mucosa.

BrdU labeling was visualized using mouse monoclonal anti-BrdU antibody (1:50; Dako, Glostrup, Denmark).[1,2] The BrdU labeling index was represented by the number of BrdU-positive cells expressed as a percentage of the total epithelial cell number in ten arbitrarily selected areas in the lesser curvature of the midantrum. The labeling index was significantly lower in the treated than the untreated group (see Table 1).

This study using the Mongolian gerbil model confirmed that eradication of *H. pylori* resulted in a significant decrease of polyp formation, inflammatory cell infiltration, and cellular proliferation in the gastric mucosa. In our previous study, gastric inflammation induced by *H. pylori* was closely related to gastric carcinogenesis.[2] Thus, *H. Pylori* eradication could diminish mucosal alterations linked to gastric carcinogenesis.

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Table 1. Histological examination of the stomachs

	BW	aHP-IgG	Polyps	IM	BrdU LI	Poly	Mono
Er(+) ($n = 6$)	112.2 ± 11.0	54.8 ± 61.2*	4.3 ± 3.8*	2.0 ± 3.2	6.3 ± 2.8*	0.67 ± 0.51*	1.17 ± 0.75*
Er(−) ($n = 5$)	112.0 ± 14.0	179.0 ± 153.4	14.8 ± 6.1	6.0 ± 2.7	17.1 ± 8.1	1.80 ± 0.45	2.80 ± 0.45
HP(−) ($n = 6$)	108.9 ± 2.6	(−)	0	0	3.6 ± 0.21	0	0

BW, body weight (g); aHP-IgG, anti-*Helicobacter pylori* IgG antibody (A.I.); polyps, the number of polyps per gerbil; IM, the number of intestinal metaplastic foveolae per gerbil; BrdU LI, 5′-bromo-2′-deoxyuridine (BrdU) labeling index; Poly, polymorphonuclear neutrophil (graded according to the Updated Sydney System); Mono, monomorphonuclear cell (graded according to the Updated Sydney System); Er(+), gerbils treated with amoxycillin and omeprazole; Er(−), untreated gerbils; HP(−), uninfected control
* Significant difference compared to Er(−) group (Mann–Whitney *U* test; *P* values <0.05 were considered to be significant)

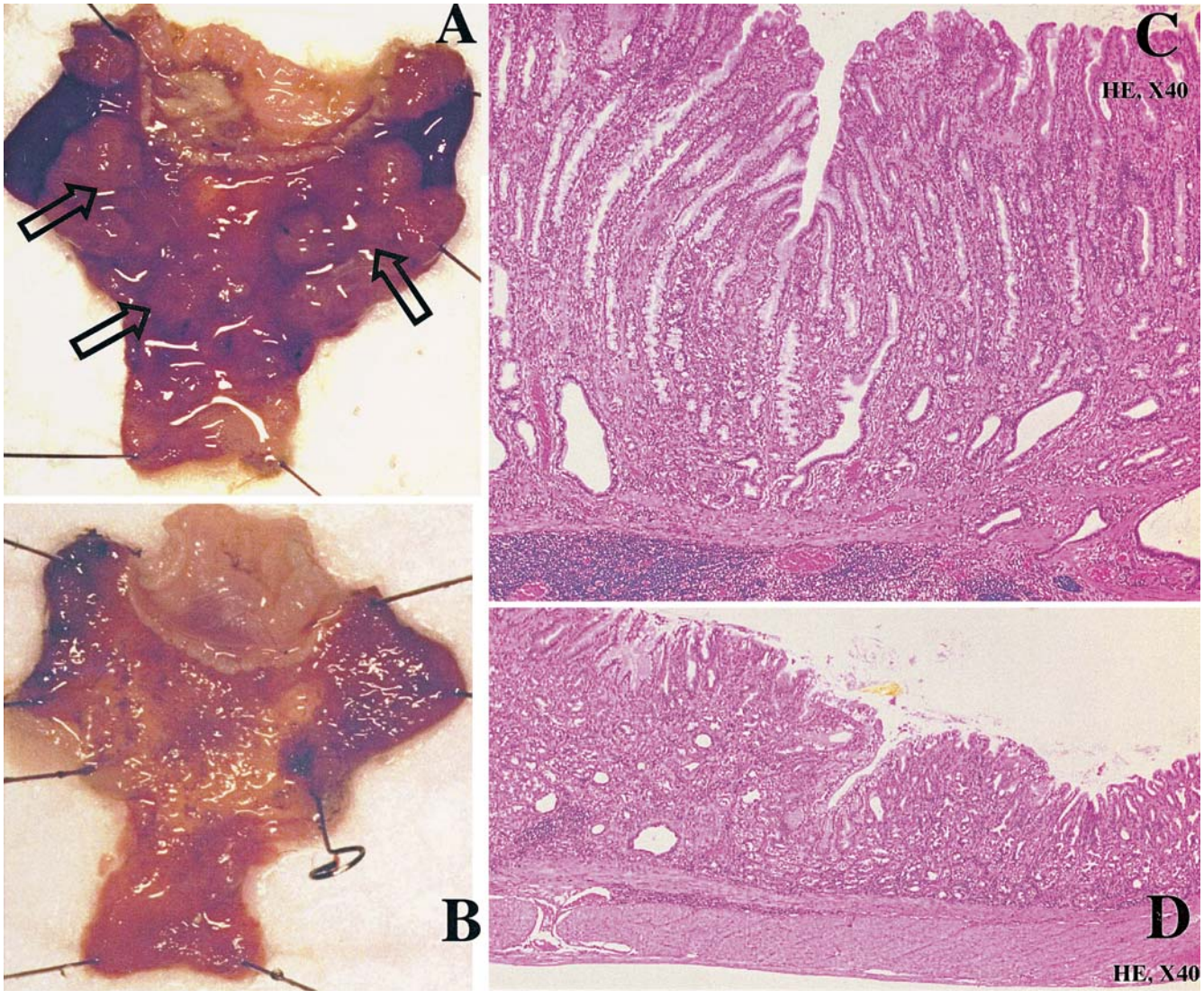

Fig. 1. The stomach in the untreated (**A**, **C**) and treated (**B**, **D**) animals. **A** Untreated animals. The antral mucosa appears thickened, and many sessile polyps (*arrows*) are found along the border between the pyloric and fundic mucosa. **B** Treated animals. Polyps are significantly fewer than in the untreated group. **C** Untreated animals. Marked cell infiltration, predominantly by lymphocytes, in the lamina propria of the pyloric mucosa. Lymphoid follicles seen in the deeper portions of the mucosa and submucosa. H&E, ×40. **D** Treated animals. The grade of inflammation of the gastric mucosa is significantly less pronounced than that in the untreated gerbils. H&E, ×40

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