Recent studies have suggested that decrease in Helicobacter pylori infection may predispose to allergic diseases. However, there are few reports of the relationships of eosinophilic gastrointestinal disorders (EGIDs), especially eosinophilic gastroenteritis (EGE), with H. pylori infection. We investigated the possible influence of H. pylori infection on EGIDs in Japanese patients. We performed a case-control study to investigate the prevalence of H. pylori infection in patients with EGIDs. Eighteen with eosinophilic esophagitis (EoE) and 22 with EGE were enrolled. For each patient, 3 age- and gender-matched normal controls (n = 120) were randomly selected from a population who received a medical check-up between April 2010 and December 2011 at the Shimane Institute of Health Science. The mean ages of the EoE and EGE patients were 50.9 ± 17 and 49.2 ± 20 years, respectively. Males were more frequently seen in the EoE group, while there was no significant gender difference in regard to EGE. Of the patients with EoE, 22.3% were infected with H. pylori, as compared to 55.5% of their age- and sex-matched normal controls. The odds ratio for EoE patients to have an H. pylori infection was 0.22 (p<0.05). In addition, 22.7% of the patients with EGE and 48.5% of their matched controls were infected with H. pylori, with odds ratio for EGE patients to have an H. pylori infection shown to be 0.31 (p<0.05). In conclusion, the prevalence of H. pylori infection was significantly lower in EGE and EoE patients in Japan as compared to normal control subjects.

Key Words: eosinophilic esophagitis, eosinophilic gastroenteritis, Helicobacter pylori infection, Th2
diagnosed as H. pylori-positive, while 55.5% of the matched controls were positive. Thus, the rate of H. pylori infection was significantly lower in patients with EoE as compared to the normal controls, while the odds ratio (OR) for those patients to be infected was 0.22 (p<0.05). As for EGE cases, 22.7% were diagnosed as H. pylori-positive, while 48.5% of the matched controls were positive, again showing a significantly lower rate of infection in patients with EGE as compared to the normal controls (Fig. 1). The OR for EGE patients to have an H. pylori infection was 0.31 (p<0.05).

Discussion

EoE and EGE are allergic digestive diseases characterized by chronic inflammation along with dense mucosal infiltration of eosinophils.\(^{(3,4)}\) Increasing numbers of patients with EoE have been reported in Western countries,\(^{(25–28)}\) while many cases of EGE have been reported in Japan.\(^{(11,12)}\) It is considered that Th2-mediated allergic response and Th2-type cytokines, including IL-5, 13, 15, and eotaxines, are involved in development of these diseases.\(^{(29–33)}\)

During an immune response, different groups of T helper (Th) cells, termed Th1 and Th2, release different patterns of cytokines. Th1 cells mediate cell-mediated immunity, as well as production of opsonizing and complement-fixing antibodies by B cells, while Th2 cells induce production of high levels of antibodies, including IgE, as well as eosinophilia. It has been speculated that particular allergic conditions such as bronchial asthma and allergic rhinitis are increasing because of an imbalance between Th1 and Th2 type immune responses due to a modern clean lifestyle,\(^{(19)}\) which is termed the hygiene hypothesis.\(^{(20)}\) Th2 cytokines suppress Th1 responses, while Th1 cytokines inhibit Th2 responses and vice versa. These systems must remain in balance to maintain a healthy condition. The immune system of neonatal humans is thought to have a Th2 bias that gradually diminishes during the first 2 years of life in non-allergic individuals.\(^{(24)}\) For development of a normal well-balanced immune system, Th1 stimulus from the environment is necessary. Without a balanced immune system, allergic diseases are prone to occur because of the continuing Th2 bias. Many bacterial infections including mycobacteria can provide such Th1 stimulus.\(^{(35)}\) However, because of improved sanitation and the reduced chance of having a bacterial infection during childhood, individuals have a higher chance to continue to with a skewed Th2 immune response.\(^{(36)}\)

H. pylori infection is considered to be an important pathogenic factor in chronic gastritis, peptic ulcer disease, gastric cancer, and MALT lymphoma.\(^{(7–9)}\) Due to improved sanitation and the reduced chance of infection during childhood, H. pylori infection is rapidly decreasing in Japan,\(^{(10–13)}\) along with peptic ulcer diseases and gastric cancers. However, this decreased rate of H. pylori infection has led to increases in cases of gastric acid secretion and gastro-esophageal reflux diseases.\(^{(17,38)}\) Moreover, recent studies have suggested that a decrease in H. pylori infections may predispose individuals to various allergic diseases.\(^{(39)}\) Th1-mediated response is activated in cases of infection, thus Th2 type immune response is expected to be continuously skewed in infected individuals, who are likely to become prone to Th2 type allergic responses. Common pathological conditions including exaggerated Th2 response to environmental and food allergens are considered to play important roles in the pathogenesis of EGIDs, and Dellon et al. recently reported that H. pylori infection was inversely associated with esophageal eosinophilic infiltration.\(^{(21)}\)

In summary, we confirmed the decreased rate of H. pylori infection in Japanese patients with EoE as compared to the control subjects. In addition, our findings are the first to show that the H. pylori infection rate is lower in EGE as well as in EoE patients. Our results are limited by the relatively small sample size, and the fact that other bacterial and viral infections were not investigated. In addition, H. pylori infection was only determined with a serum antibody test. The specific role of the decreased rate of H. pylori infection should be confirmed in a larger scale prospective study.

### Table 1. Clinical characteristics of enrolled subjects

|             | Cases | Control | Cases | Control |
|-------------|-------|---------|-------|---------|
| No. of cases | 18    | 54      | 22    | 66      |
| Male/Female | 11/7  | 33/21   | 12/10 | 36/30   |
| Mean age ± SD (years) | 50.9 ± 17.4 | 50.5 ± 16.5 | 49.2 ± 20.0 | 49.4 ± 18.4 |

**Fig. 1.** The H. pylori infection rate was significantly lower in patients with EoE and EGE as compared to their respective age- and gender-matched controls. *Significantly different as compared with control (p<0.05).
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Conflict of interest

No potential conflicts of interest were disclosed.