in gastric mucosa can be determined (8). Mononuclear cells of H. pylori-positive gastric mucosa were found to actively produce H. pylori-specific antibodies (IgA ELISPOT; 838 cells/10^6 MNC, IgG ELISPOT; 366 cells/10^6 MNC, n=34). These ELISPOT numbers correlate with the histological grade of gastritis. Thus, the inflammatory infiltrate is considered to be a specific response against H. pylori infection.

Next, we investigated whether these H. pylori-specific antibodies in gastric mucosa and/or neutrophils are responsible for cytotoxicity to epithelial cells. Soluble H. pylori antigen, IgG type H. pylori antibody and neutrophils are the three factors which were required to induce the cytotoxicity, the vacuolation of cultured Vero cells in vitro. Immune complex formed with H. pylori antigen and the antibody induced the superoxide production of neutrophils. The addition of human recombinant superoxide dismutase (SOD) to the culture inhibited the vacuolation of Vero cells induced by the above three factors. These observations suggest that superoxide, produced from the neutrophils stimulated with H. pylori antigen and antibody immune complex, might be the final cytotoxic agent to epithelial cells. We emphasize that the immunological interactions may be associated with the pathophysiology of type B gastritis positive for H. pylori.

**References**


3. **Inflammatory Bowel Disease and Immunology**

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**Key words:** inflammatory bowel disease, ulcerative colitis, Crohn’s disease

**Inflammatory bowel disease and immunology**

Ulcerative colitis (UC) and Crohn’s disease (CD) are collectively called (idiopathic) inflammatory bowel disease (IBD), and treated as a single group in practice. However, in recent years, detailed analysis of the clinical pictures of the diseases and immunological studies of their pathogenesis suggested that UC and CD are different from each other both clinically and pathophysiological. Recent advances in immunology and molecular biology have greatly contributed to this renewed understanding of the diseases (1, 2).

UC is a diffuse, chronic, non-specific inflammatory disease which mainly affects the mucosa and forms erosion and ulcers. It is intractable with alternating phases of remission and relapse. The colonic mucosal lesions are markedly infiltrated with lymphocytes, plasma cells, macrophages and other immunocompetent cells, suggesting that an immunological mechanism is involved in the development of the disease as well as in its persistence and progress to a chronic state.

One recent topic is the finding that HLA-DR antigen, a class II MHC which is not expressed in the colonic mucosal epithelium of healthy people, was detected in epithelial cells of the colonic mucosa of patients with UC. Activated T cells, B cells, macrophages and neutrophils were found in the lesions. It is also known that adhesion molecules, accessory molecules which appear when macrophages present antigens, are expressed.

The pathogenic mechanism of the mucosal lesions in UC is believed to be mediated by IL-1, other cytokines, oxygen radicals, PAF, LTB4 and other chemical mediators.

CD mainly affects young adults. It presents granulomatous inflammatory lesions with accompanying fibrosis and ulceration, and its clinical picture is very diverse. Attention has been directed to functional abnormalities of macrophages in CD in relation to the immunological modifications. CD differs immunologically from UC in antigen proteins corresponding to blood antibodies and in IgG subclasses of antibody producing cells.

From these results, the etiology of inflammatory bowel...
diseases still remains to be clarified. Our hypothesis is as follows (Fig. 1).

At first, inflammatory change occurs in colonic mucosa in genetically predisposed patients, which allows massive infiltration of antigens (enterobacterial, dietary and/or self antigens) into the mucosa. Continuous activation of macrophages, T cells and/or B cells results in the overproduction of inflammatory and regulatory cytokines, such as IL-1, IL-2, IL-6, etc. An elevated ratio of CD4/CD8 in the lamina propria represents hyperimmune status in the mucosa, and is likely to stimulate B cells to produce antibodies including anti-colon antibodies. Colonic epithelial cells and monocytes in the mucosa express HLA-DR through the stimulation of cytokines (interferon-γ), and show antigen-presenting property, which leads mucosal inflammation to complexed and more continuous one (3-5).

Overexpressed cell adhesion molecules (6) play an important role in the infiltration of neutrophils and lymphocytes into the mucosa, which induces mucosal damage of IBD by producing chemical mediators and oxygen radicals. Impaired blood perfusion through the damage to vascular endothelial cells of mucosal capillaries is also important.

Various processes are mixed and contribute to the specific features of IBD.

References