Gastric mucosal disease

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Chapter 7

Summary
The discovery of *Helicobacter pylori* in 1983 by Warren and Marshall has opened a new era for the gastrointestinal disease. This organism is accepted as the causative agent of gastritis, peptic ulcer, gastric carcinoma, MALT lymphoma and other diseases. *Hp* related diseases could also be among the most prevalent in the world. **Chapter 1** of this thesis gives an introduction and some background information of *Helicobacter pylori* and its related diseases.

**Chapter 2** investigates 1991 *H.Pylori*-infected patients from nine countries. The Hematoxylin-eosin stained biopsies from antrum and corpus were scored semi-quantitatively according to the updated Sydney system. Particular attention was paid to the glandular atrophy and intestinal metaplasia (IM) in antrum biopsies. An analysis of atrophy in the different groups of patients showed significant differences in the antral mucosa. Highest scores for antrum atrophy were found in New Orleans blacks and in Japanese patients, and slightly lower scores in patients from Colombia. Lower scores were seen in three cities from China: Xi-an, Shanghai and GuangZhou. The lowest scores were found in four European countries: Portugal, the Netherlands, Finland and Germany, and especially in Thailand. As for intestinal metaplasia, the score is generally low except for Xi-an, Japan and Shanghai. The scores of atrophy and intestinal metaplasia both increased with the age in almost all investigated groups. Our finding reveal substantial geographical differences in the age-related degree of atrophy and intestinal metaplasia. The overall prevalence of atrophy and intestinal metaplasia mirrored the respective incidence of gastric cancer and atrophy, intestinal metaplasia
appeared at younger ages in populations at high risk for gastric cancer than in those at low risk.

The morphological criteria for classification and grading of chronic gastritis remain obscure and poorly standardized, especially with respect to atrophy. Since the updated Sydney system was introduced in 1994, a new visual analogue scale for grading morphological variables was available. Several studies on interobserver variation in the assessment of atrophy were reported, but the result is still not good; the agreement between the different observers is poor to moderate. **Chapter 3** investigates the degree of agreement between the endoscopic atrophic border (EAB) and the histological score for atrophy. During the endoscopy, the grade of gastric atrophy was estimated according to EAB. Antral and corpus biopsies from 298 dyspeptic Japanese patients were taken and the score of atrophy was evaluated semi-quantitatively according to the updated Sydney classification system. Our study shows that the degree of agreement between the endoscopic score of atrophy (EAB) and the histological score of atrophy was good with a weighted kappa value of 0.51 (95% confidence interval 0.44-0.59). It is better than interobserver histological agreement between two pathologists. It is known that the biopsy specimens from one site in the stomach only represent the local findings; the biopsy may not reveal the true extent of gastritis. Histologic atrophy may be absent when endoscopic atrophy is present, and vice versa. The diagnosis of atrophic gastritis should be made on the basis of both endoscopy and histology. As more endoscopists and pathologists get to know the criteria well, a higher degree of agreement on atrophy has become possible.
Invasion and metastasis are two important malignant phenotypes. The mechanism of tumor invasion and metastasis is complex and not well understood. Chapter 4 reports the expression of one of the cysteine proteinase – Cathepsin B (CB) in the human gastric carcinoma. CB is a lysosomal proteinase that functions in the normal turnover of cell protein. It can degrade several extracellular matrix components. We use anti-CB antibody for immunohistochemistry and cDNA of CB for in situ hybridization and dot blot method to study its expression in both protein and mRNA levels. CB overexpression was found in gastric carcinoma when compared with normal mucosa. Diffuse cytoplasmic CB staining at both mRNA and protein were identified in malignant cells of 53.3% and 69.1% of gastric carcinoma respectively. The increased staining of CB in malignant cells was associated with the depth of the invasiveness and the growth pattern as well as the metastasis of lymph nodes, but not with the histological classification. That means: the expression of CB in the infiltrative type is higher than that in the expanding type; higher in advanced type than that in early type; higher when metastatic lymph nodes were present than in cases without metastasis. Our findings indicate that CB expression is upregulated in human gastric carcinoma and correlated with tumor progression. CB expression was also found in the endothelial cells of the microvessels that correlated with the angiogenesis. The study suggests that CB contributes to the development of the invasive phenotype and angiogenesis. Defining the role of CB in the invasiveness of gastric tumor is important with regard to understanding the biology of this process as well as in search for potential prognostic markers and targets for therapeutic intervention.
Gastric acid secretion represents the outcome of several regulatory signals. It includes central and peripheral regulation. The latter involves neural, endocrine and paracrine pathways. It has been reported that three important endocrine cells are related to the gastric acid secretion—Gastrin (G) cell of the antrum, somatostatin (D) cells of the fundus and antrum, and ECL cell of the fundus. They either upregulate or downregulate acid secretion by the parietal cells. Chapter 5 reviews the regulation and effect of these three important endocrine cells on gastric acid secretion and their pathologic situation.

As described previously, Gastrin G cells and Somatostatin D cells are important regulators of gastric acid secretion. The alteration between gastrin and somatostatin plays a key role in gastroduodenal disease. Several factors including *H. pylori* infection can interfere with this physiological balance, resulting in disturbances in gastric acid secretion. Chapter 6 investigates the expression of G cells and D cells in antrum and corpus biopsies from 122 individuals with dyspeptic complaints; the relation between their expression and *H. pylori* status is specifically compared. Two antrum and two corpus biopsies were taken during upper endoscopy and evaluated semi-quantitatively according to the updated Sydney system. To evaluate the amount and distribution of neuro-endocrine cells, especially gastrin G cells and somatostatin D cells, additional immunohistochemical stains were used. All subjects were divided into three groups: patients with *Hp* positive gastritis, with *Hp* negative gastritis and histological normal stomach. It was found that the amount of G cells was significantly higher in patients with *Hp* positive gastritis when compared with the *Hp* negative and normal groups. And this elevation is associated with the severity of *Hp* colonization. In contrast, the amount of D
cells was significantly lower in the _Hp_ infected group than in either non-infected or normal individuals. In _Hp_ positive subjects, the percentage of G cells is elevated while the percentage of D cells is decreased significantly. The results strongly suggest the relative hypofunction of the inhibitory action of D cell against G cells and the hyperfunction of the stimulating action of G cells itself may be responsible for increased gastric acid output.