

## Ciliated Gastric Cells among Japanese Living in Hawaii

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A total of 129 consecutive gastrectomy specimens from Japanese (99), Philipinos (11), Hawaiians (8), Koreans (5), Chinese (4) and Caucasians born in Hawaii (2) were examined under high-power light microscopy (1000 $\times$ ) for the presence of ciliated gastric cells. Fifty-two of the 129 gastrectomy specimens (40.3%) contained ciliated cells. Ciliated cells were found in the basal segments of antral glands (usually cystically dilated) whose superficial segments had undergone intestinal metaplasia. The presence of ciliated cells in the gastric mucosa was influenced by the age of the patient and by the degree of intestinal metaplasia: the older the patient, the greater the degree of intestinal metaplasia and the greater the frequency of specimens with ciliated cells. The presence of ciliated cells was also influenced by the type of lesion in the specimen. Although the highest frequency (47.2%) was found in stomachs removed for adenocarcinoma, a substantial number of stomachs removed for gastric ulcer also showed that change (36%). The data suggest that increasing age and advanced atrophic gastritis, especially of the antrum, provide the necessary conditions that lead to the development of cilia, not only in Japanese subjects, but in other Hawaiian ethnic groups as well.

Key words: Gastric mucosa — Ciliated cells

Until a few years ago, gastric ciliated metaplasia was considered a rare phenomenon. Up to 1983, only six cases with ciliated cells in the gastric mucosa had been reported in the literature.<sup>1-3</sup> In that year, two independent studies<sup>4,5</sup> indicated that ciliated cells in the gastric mucosa occurred more commonly than had previously been thought. In fact, Stemmermann *et al.*<sup>5</sup> estimated that approximately 10% of the stomachs of Japanese patients in Hawaii have gastric cysts lined with ciliated cells. In 1986,<sup>6</sup> we demonstrated ciliated gastric cells in 35% of 137 consecutive gastric specimens from Japanese patients living in Japan having either chronic peptic ulcer, adenoma or intramucosal carcinoma. Recently, Torikata *et al.*<sup>7</sup> found ciliated cells in 46% of 50 consecutive gastrectomies performed on Japanese subjects living in Japan.

For some years, we have been looking for ciliated cells in gastric specimens from European and American patients. Three cases among Europeans were found: one in a Norwegian patient with adenocarcinoma of intestinal type,<sup>8</sup> one in a Swedish patient with extended flat tubular adenoma<sup>9</sup> and one in an English patient with adenocarcinoma (Rubio and Filipe, unpublished data). In addition one case of ciliated gastric metaplasia was found in a Caucasian American<sup>10</sup> in dilated gastric glands underneath a gastric adenoma. The apparent rarity of gastric ciliated metaplasia among Caucasians and its high frequency among patients of Japanese ancestry, suggested differences in the "normal" gastric mucosa in the two ethnic groups.

In previous reports, the possible association between ciliated cells and intestinal metaplasia of the stomach was pointed out.<sup>5,6</sup> The purpose of the present study was to correlate the presence of ciliated gastric cells to the degree of intestinal metaplasia in consecutive gastrectomy specimens received at this department between 1985 and 1988.

### MATERIALS AND METHODS

We studied 130 serially accessional gastrectomy specimens received at the Department of Pathology, Kuakini Medical Center, between 1985 and 1988. The freshly resected stomach was processed as reported elsewhere.<sup>11,12</sup> Briefly, it was opened along the greater curvature, pinned to a slab of paraffin and fixed in 10% buffered formalin. The preparation was placed in a refrigerator for 12 h. After removing the paraffin slab, the specimen was transferred to a plastic bag containing 500 ml of a substrate to demonstrate the presence of alkaline phosphatase<sup>11</sup> and incubated at 37°C for 1 h. After this procedure, the specimen was washed in tap water and photographed. Mucosal surfaces stained red by this procedure consisted of metaplastic intestinal epithelium. The mucosal strips from the lesser and greater curvature were sampled for histological examination in pieces of about 4 cm in length. Samples were also removed from the junction zone as well as from the anterior and the posterior wall.

The extent of intestinal metaplasia was graded macroscopically as grade 0 = none; grade 1 = widely spaced foci of intestinalization; grade 2 = separate foci in every microscopic field or in every 1 cm<sup>2</sup> of the gross specimen;

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grade 3=confluent intestinalization.<sup>11, 13)</sup> Histological sections were scrutinized at high power (1000× oil immersion) for the presence of ciliated gastric cells. Special attention was paid to the presence of gastric cysts, particularly those in the antral region. The microscopical study was then done without knowledge of the patient's sex, age or racial background.

The preparations had been stained with hematoxylin and eosin. In five cases, sections were stained with con-canavallin A, Grimelius or Masson trichrome stains, to reinforce the staining of the cilia as reported elsewhere.<sup>14)</sup>

## RESULTS

One of the 130 resected specimens was a re-resection carried out in a patient in whom a distal subtotal gastrectomy for cancer stage I had been performed 16 years previously. The specimen consisted of the proximal 20% of the stomach. This case was rejected from the present study. Data regarding the findings in the remaining 129 patients are presented in Tables I-V.

**Specimens having gastric ciliated cells** Fifty-two of the 129 gastrectomy specimens (40.3%) contained ciliated cells.

**Topographic localization of ciliated cells** Ciliated gastric cells were usually found in the cystically dilated glands of the antral mucosa. The superficial segments of those glands had usually undergone intestinal metaplasia.

Ciliated cells were usually found in clusters of antral glands with cystic dilation. In some specimens, however, only isolated dilated glands with ciliated cells were observed. The cysts with ciliated cells were generally arranged in rows or in clusters. Less frequently, isolated antral cysts containing ciliated cells were observed. In some cysts, more than 90% of the cells were ciliated (Fig. 1), while in others the proportion of ciliated cells was less than 10%.

**Age and ciliated gastric cells** The results in Table I show that the proportion of specimens with ciliated cells increased with age; for patients above 70 years of age, the frequency of ciliated metaplasia was about twice as high as for those 59 years of age or less. The mean age among

Table I. The Age of the Patient and the Presence of Ciliated Metaplasia in 129 Gastrectomy Specimens

Age	No. of patients with ciliated metaplasia (%)	Total no. of patients
< 49	2 (25.0)	8
50-59	5 (26.3)	19
60-69	13 (34.2)	38
70-79	22 (51.2)	43
> 80	10 (47.6)	21
All	52	129

Table II. Race, Birthplace and the Presence of Ciliated Metaplasia in 129 Gastrectomy Specimens

Race	Total	No. of patients with ciliated metaplasia (%)	Hawaiian-born	No. of patients with ciliated metaplasia (%)	Foreign-born	No. of patients with ciliated metaplasia (%)
Japanese	99	46 (46.4)	85	41 (48.2)	14	5 (35.7)
Philippines	11	1 (9)	2	0 (0)	9	2 (22.2)
Hawaiian	8	3 (37.5)	8	3 (37.5)	0	0
Chinese	4	0 (0)	4	0 (0)	—	—
White	2	1 (50)	2	1 (50)	0	0
Korean	5	1 (20)	1	1 (100)	4	0
Total	129	52 (40.3)	102	46 (45.1)	27	7 (25.9)

Table III. The Degree of Intestinal Metaplasia and the Presence of Ciliated Metaplasia in 129 Gastrectomy Specimens

	Intestinal metaplasia score				
	0	1	2	3	
No. of gastrectomies with ciliated metaplasia (%)	0 (0)	14 (29)	32 (60)	6 (66.6)	52 (40.3)
Total	18	49	53	9	129

Table IV. The Histologic Diagnosis and the Presence of Ciliated Metaplasia in 129 Gastrectomy Specimens

Histologic diagnosis	No. of gastrectomies with ciliated metaplasia (%)	Total
Adenocarcinomas	42 (47.5)	89
Hyperplastic polyp	1 (33.3)	3
Lymphosarcoma	0 (0)	2
Ulcer (gastric)	9 (36)	25
Ulcer (duodenal)	0 (0)	10
All	52	129

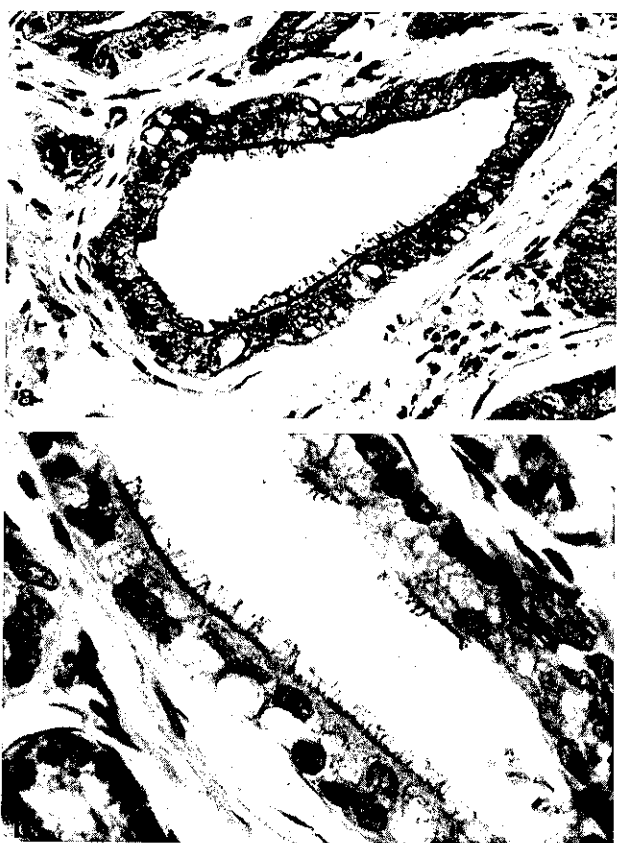


Fig. 1. a) Cystically dilated pyloric gland with cilia in the free border of the cytoplasm (Masson-trichrome  $\times 100$ ). b) Detail from a) to demonstrate well-defined ciliated cells (Masson-trichrome  $\times 400$ ).

cilia and among females 20 (42%) had cilia. Thus, no difference due to sex was found.

**Race and ciliated gastric cells** The majority (99 of 129) of patients were Japanese (Table II). In 46 instances (46.4%), the resected stomachs contained ciliated cells. It is of interest to point out that 85 of the 99 Japanese patients had been born in Hawaii and 41 of these (48.2%) had ciliated cells. Ciliated gastric cells were also found in specimens from Philipinos, Hawaiians, Koreans and Whites born in Hawaii.

**Intestinal metaplasia and gastric ciliated cells** The presence of ciliated gastric cells was correlated with the extent of intestinal metaplasia recorded at macroscopical examination (Table III). The results of this study demonstrated that of the 67 specimens with slight (Grade I) intestinal metaplasia in Table I, 14 (20.9%) had ciliated gastric cells. On the other hand, of the 62 specimens with moderate or severe intestinal metaplasia (scores 2 and 3 in Table IV), 38 (or 61.3%) had cilia in the resected stomach.

**Ciliated gastric cells and other gastric pathology** Of the 89 gastric carcinomas in Table IV, 42 (47.2%) had ciliated cells in the non-involved gastric mucosa. In nine of the 25 specimens with a gastric ulcer (36%) ciliated gastric cells were found. Ciliated gastric cells were also present in one resected stomach containing an hamartomatous polyp.

#### DISCUSSION

The results of the present work indicate that 52 of the 129 gastrectomy specimens examined (40.3%) contained ciliated cells. The majority of the specimens (99 of 129) were from Japanese patients, either emigrants to Hawaii (14 patients) or born in Hawaii (85 patients). The frequency of ciliated gastric cells in overt carcinoma in this study was similar to that found among Japanese subjects living in Japan having microinvasive carcinomas.<sup>7)</sup> In that study, 35% of the 137 consecutive gastric specimens revealed ciliated cells, the highest percentage being found in specimens having concomittantly a gastric adenoma (42.6%), or an intramucosal adenocarcinoma of intestinal type (41.6%), followed by intramucosal adenocarcinoma of diffuse type (15.4%) and by chronic peptic ulcer (16%). Japanese ethnicity was not indispensable for the development of ciliated cells, since the phenomenon was also present among other patients living in Hawaii, such as Polynesians, Philipinos, Koreans and Whites born in Hawaii. These results suggest that there are environmental factors in Hawaii similar to those present in Japan that favor the development of ciliated cells of the stomach.

The presence of ciliated cells in the gastric mucosa was apparently influenced by the age of the patient and by the

patients with ciliated metaplasia was 72 years, while that for patients without cilia was 66 years.

**Sex and ciliated gastric cells** Of the 129 patients, 77 were males and 52 females. Among males, 30 (46%) had

degree of intestinal metaplasia; the older the patient, the greater the degree of intestinal metaplasia, and the greater the frequency of specimens with ciliated cells. On the other hand, studies on gastrectomy specimens in elderly Swedish patients having widespread intestinal metaplasia, demonstrated the absence of ciliated gastric cells (unpublished data). This suggests that there are local environmental factors in Hawaii and Japan that favor the development of cilia and that they are not present in Sweden to the same degree.

The highest frequency of patients with cilia was found among cases with carcinoma. Specimens containing gastric ulcer also exhibited ciliated gastric cells. Ciliated cells were not found in cases with lymphosarcoma or duodenal ulcer.

Ciliated gastric cells were found in cystically dilated pyloric glands.<sup>5,6</sup> It has been proposed that cilia represent an adaptation of pyloric cells to mucous retention in cystically dilated glands,<sup>15</sup> although not all ciliated cells were found in cystically dilated glands. Previous

studies<sup>15</sup> with semiserial sections have demonstrated that cysts are part of a complex intercommunicating system in the gastric mucosa. The cilia of undilated glands may be found in cul-de-sacs in that interconnecting system.

Ultrastructural studies have shown that cilia are associated with long, branching compound microvilli<sup>5</sup> resembling those of the epididymis and pleural mesothelioma; indicating that they are part of a complex structural change.

Studies in progress<sup>16</sup> will elucidate whether cystic dilatation and ciliated cells are a reflection of differences in the sensitivity of the gastric mucosa to the action of environmental gastric carcinogens present in different geographical areas.

#### ACKNOWLEDGMENTS

This study was supported by grants from the Swedish Society of Medicine and the Swedish Cancer Fund.

(Received July 23, 1990/Accepted October 19, 1990)

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