田久保海誉退職記念国際シンポジウム
東京食道研究デー 2015

International Symposium
Tokyo Esophageal Research Day, 2015,
To Commemorate the Retirement of Dr. Kaiyo Takubo

2015年5月9日(土) 都市センターホテル

Saturday, 9 May 2015　at Toshi Center Hotel Tokyo

Program

10：25〜10：30	**1. Opening remarks** 開会のご挨拶	Kaiyo Takubo, MD, PhD 田久保海誉
10：30〜12：05	**2. Recent advances of esophagology in Japan** 最近の日本における食道学の進歩	
（10：30〜10：50）	**2-1**	**How to decide the spatial distribution of the location of a small lesion in the lower esophagus?** Moderator: Harushi Udagawa, MD, FACS. Department of Gastroenterological Surgery, Toranomon Hospital 宇田川 晴司 先生 国家公務員等共済組合連合会虎の門病院消化器外科部長 Speaker: Yoshio Hoshihara, MD. Health Support Center, the Ministry of Economy, Technology and Industry, Japan 星原 芳雄 先生 経済産業省診療所所長
（10：50〜11：05）	**2-2**	**Detailed features of palisade vessels in the esophagogastric junction revealed by magnifying endoscopy** Moderator: Harushi Udagawa, MD, FACS. Department of Gastroenterological Surgery, Toranomon Hospital 宇田川 晴司 先生 国家公務員等共済組合連合会虎の門病院消化器外科部長 Speaker: Youichi Kumagai, MD. Department of Digestive Tract and General Surgery, Saitama Medical Center, Saitama Medical University, Saitama 熊谷 洋一 先生 埼玉医科大学国際医療センター消化器一般外科准教授
（11：05〜11：30）	**2-3**	**Use of four unique features, including palisade veins, as histologic markers allows confirmation of esophageal origin in EMR and ESD specimens from the columnar-lined esophagus** Moderator: Yuichi Ishikawa, MD. Division of Pathology, The Cancer Institute, Japanese Foundation for Cancer Research, Tokyo, Japan 石川 雄一 先生 公益財団法人 がん研究会がん研究所病理部部長 Speaker: Junko Aida, DDS, PhD. Research Team for Geriatric Pathology, Tokyo Metropolitan Institute of Gerontology 相田 順子 先生 東京都健康長寿医療センター研究所老年病理学研究チーム副部長

（11：30～11：50）	**2-4**	**Clinicopathologic characteristics of basaloid squamous carcinoma of the esophagus** Moderator: Kenichi Ohashi, MD, PhD. Professor, Pathology Department, Yokohama City University School of Medicine, Yokohama, Japan **大橋 健一 先生** **横浜市立大学医学部病態病理学教授** Speaker: Tomio Arai, MD. Department of Pathology, Tokyo Metropolitan Geriatric Hospital **新井 冨生 先生** **東京都健康長寿医療センター病理診断科部長**
（11：50～12：05）	**2-5**	**Endocytoscopic observation of various esophageal lesions** Moderator: Zenya Naito, MD, PhD. Professor and Chairman, Department of Integrated Diagnostic Pathology, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan **内藤 善哉 先生** **日本医科大学大学院統御機構診断病理学教授** Speaker: Youichi Kumagai, MD. Department of Digestive Tract and General Surgery, Saitama Medical Center, Saitama Medical University, Saitama **熊谷 洋一 先生** **埼玉医科大学国際医療センター消化器一般外科准教授**
12：05～13：20	Lunch Break **昼食**	
13：20～14：10	**3. Barrett low-grade dysplasia: a relevant finding or innocent bystander?** Moderator: Takashi Yao, MD, PhD. Professor and Chairman, Department of Human Pathology, Juntendo University Graduate School of Medicine, Tokyo, Japan **八尾 隆史 先生** **順天堂大学医学部人体の生命機能人体病理病態学教授** Speaker: Professor Michael Vieth Institut für Pathologie, Klinikum Bayreuth GmbH, Preuschwitzer Str. 101, 95445 Bayreuth, Germany	

14：10〜15：00	**4. Iatrogenic pathology of the upper gut** Moderator: Tetsuo Ushiku, MD. Department of Pathology, Graduate School of Medicine, The University of Tokyo **牛久 哲男 先生** **東京大学大学院医学系研究科人体病理・病理診断学准教授** Speaker: Professor Gregory Y. Lauwers, Vice Chairman, Department of Pathology, Director, Gastrointestinal Pathology Service, Massachusetts General Hospital, Professor of Pathology, Harvard Medical School, Boston, MA, USA
15：00〜15：20	Break
15：20〜16：10	**5. Handling *Helicobacter*-negative gastritis** Moderator: Kiyoko Oshima, MD, PhD. Associate Professor and Program Director, Gastrointestinal/Liver Pathology Fellowship, Medical College of Wisconsin, USA Speaker: Professor Robert Riddell Mount Sinai Hospital, Joseph and Wolf Lebovic Health Complex, 6-502-4, 600 University Avenue, Toronto, Ontario, Canada
16：10〜17：00	**6. Do the different definitions of Barrett's esophagus destroy friendships, or can friends overcome these differences?** Moderator: Tomio Arai, MD. Department of Pathology, Tokyo Metropolitan Geriatric Hospital **新井 冨生 先生** **東京都健康長寿医療センター病理診断科部長** Speaker: Professor Henry Appelman Department of Pathology, M.R. Abell, Professor of Surgical Pathology, Director of GI Pathology Fellowship, University of Michigan. Ann Arbor, MI 48109 USA. President of US and Canadian Academy of Pathology 2006-2007.
17：00〜17：30	**7. The education of a young pathologist: A professional debt of gratitude to influential pathologists and clinicians** Moderator: Ken-ichi Mafune, MD. Division of General and Gastrointestinal Surgery, Mitsui Memorial Hospital, Tokyo, Japan **真船 健一 先生** **三井記念病院総合消化器外科部長** Speaker: Kaiyo Takubo, MD. Research Team for Geriatric Pathology, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan **田久保 海誉** **東京都健康長寿医療センター研究所老年病理学研究チーム**

17：30〜18：00	**8. History of the Japanese Society for Esophageal Diseases and the Japan Esophageal Society** Moderator: Tatsuyuki Kawano, MD. Professor, Department of Surgery, Tokyo Medical and Dental University, Tokyo, Japan **河野 辰幸 先生** **東京医科歯科大学医学部食道・一般外科学教授** Speaker: Misao Yoshida, MD. Director General, the Foundation for Detection of Early Gastric Carcinoma, Tokyo, Japan **吉田 操 先生** **早期胃癌診断協会理事長**
18：00	**9. Closing remarks　閉会のご挨拶** Robert Riddell, MD.
18：05〜	**Get-together Party** **Speech** 1. Hideki Ito, MD. Director General and President of Tokyo Metropolitan Medical Center and Research Institute of Gerontology, Tokyo 2. Misao Yoshida, MD. Director General, the Foundation for Detection of Early Gastric Carcinoma, Tokyo 3. Tamao Endo, PhD. Vice Director, Tokyo Metropolitan Research Institute of Gerontology, Tokyo **Speech and toast proposal** 4. Henry Appelman, MD. Professor, Department of Pathology, M.R. Abell, Professor of Surgical Pathology, Director of GI Pathology Fellowship, University of Michigan **Speech of gratitude** 5. Kaiyo Takubo, MD.

Abstracts

Abstract 2-1

How to decide the spatial distribution of the location of a small lesion in the lower esophagus?

Yoshio Hoshihara, MD

Health Support Center, the Ministry of Economy, Technology and Industry, Japan

For a short time before the presentation of the above problem, I would like to mention our study that showed the lower end of the lower esophageal longitudinal palisade veins is the endoscopic landmark of the EGJ.

Background: Several investigators revealed that the majority of neoplastic lesions in SSBE were endoscopically found between the 12 o'clock and 5 o'clock locations. In their articles, some authors described that the 3 o'clock position was defined as alignment with the lesser curvature of the stomach, but another claimed that the 3 o'clock position corresponded to the posterior wall of the esophagus.
Aim: To clarify the 3 o'clock position corresponds to where at the gastric cardia in conventional endoscopy.
Patients: A total of 30 patients were consecutively examined by upper GI endoscopy. The patients with surgical treatment of upper GI tract were excluded.
Methods: After the observation of the lower esophagus, an endoscope was inserted into the stomach and pulled up into the esophagus observing the posterior wall at the 6 o'clock position. Many still pictures were taken at the gastric cardia and the lower esophagus, and a video image of this procedure was also recorded on DVD.
Result: We could set the 6 o'clock position to correspond to the posterior wall at the gastric cardia by using the procedure described above. Then in this setting the 3 o'clock position corresponded to the lesser curvature of the stomach. The error arising from this procedure was about 30 degree (1 hour).
Further large investigation should be necessary to establish landmarks which are useful to decide the spatial direction of a lesion in the lower esophagus.

Abstract 2-2

Detailed features of palisade vessels in the esophagogastric junction revealed by magnifying endoscopy

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2) Department of Surgery, Ohta Nishinouchi Hospital, Fukushima, Japan
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Background and study aims: The palisade vessels present at the distal end of the esophagus are considered to be a landmark of the esophagogastric junction and indispensable for diagnosis of Barrett's esophagus on the basis of the Japanese criteria. Here we clarified the features of normal palisade vessels at the esophagogastric junction using magnifying endoscopy.

Patients and methods: We observed palisade vessels in 15 patients undergoing upper gastrointestinal endoscopy using a GIF-H260Z instrument (Olympus Medical Systems Co., Tokyo, Japan). All views of the palisade vessels were obtained at the maximum magnification power in the narrow-band imaging mode. We divided the area in which palisade vessels were present into three sections: the area from the squamo-columnar junction (SCJ) to about 1 cm orad within the esophagus (Section 1), the area between sections 1 and 3 (Section 2), and the area from the upper limit of the palisade vessels to about 1 cm distal within the esophagus (Section 3). In each section, we analyzed the vessel density, caliber of the palisade vessels, and their branching pattern.

Results: The vessel density in sections 1, 2, and 3 was 9.1±2.1, 8.0±2.6 and 3.3±1.3 per high-power field (mean±SD), respectively, and the differences were significant between sections 1 and 2 ($P=0.0086$) and between sections 2 and 3 ($P<0.0001$). The palisade vessel caliber in sections 1, 2 and 3 was 138.5±58.3 μm, 166.4±63.2 μm, and 223.7±83.9μm (mean±SD), respectively, and the differences were significant between sections 1 and 2, and between sections 2 and 3 ($P<0.0001$).

With regard to branching form, the frequency of branching was highest in section 1, and the 'normal Y' shape was observed more frequently than in sections 2 and 3. Toward the oral side, the frequency of branching diminished, and the frequency of the 'upside down Y' shape increased. The differences in branching form were significant among the three sections ($P<0.0001$).

Conclusion: These results indicate that the density of palisade vessels is highest near the SCJ, and that towards their upper limit they gradually become more confluent and show an increase of thickness. Within a limited area near the SCJ, observations of branching form suggest that palisade vessels merge abruptly on the distal side. We demonstrated that palisade vessels are useful marker for endoscopic recognition of the lower esophagus.

Use of four unique features, including palisade veins, as histologic markers allows confirmation of esophageal origin in EMR and ESD specimens from the columnar-lined esophagus

Junko Aida, Makoto Nishimura, Tomio Arai, Kaiyo Takubo

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Palisade vessels locate in the lower esophageal sphincters, and their lower margin is usually defined as the esophagogastric junction (EGJ) endoscopically, in Japan. We tried this structure to apply histologic diagnosis of columnar lined esophagus (CLE) in biopsy or endoscopic specimens (EMR, ESD). Palisade vessels were defined histologically as veins more than 100 μm in size in and above the original muscularis mucosae. These veins were observed in 71% of CLE specimens (n=66) and never seen in EMR specimens from the stomach or in the middle esophagus. Esophageal glands proper and/or ducts, squamous islands, and double muscularis mucosae were seen in 56%, 53%, and 79%, respectively. At least one of these four markers was seen in 97%. Therefore, by using the palisading veins as 4th histologic marker of EGJ in endoscopic specimens, their origin from CLE were confirmed in almost all cases on the basis of histologic examination alone.

Clinicopathologic characteristics of basaloid squamous carcinoma of the esophagus

Tomio Arai, Junko Aida, Ken-ichi Nakamura, Yasuko Ushio, Kaiyo Takubo

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Basaloid squamous carcinoma (BSC) of the esophagus is a rare but distinct variant of esophageal carcinoma, identical to BSC of the upper aerodigestive tract. The incidence of BSC has been reported to present 0.4% to 3.6% of total esophageal malignant tumors. The average age of BSC patients was 64 years, ranging from 42 to 87 years, with male predominance (male to female ratio, 6.8:1). The tumor preferentially occurs in the middle part of the thoracic esophagus and appears a subepithelial tumor-like or polypoid elevation in early stages. Histologically, it is composed of basaloid cells with oval to round nuclei and scant basophilic cytoplasms, which show a solid growth pattern, small gland-like spaces, and foci of comedo-type necrosis with hyalinized stroma mimicking basement membrane. BSCs are commonly associated with intraepithelial neoplasia or invasive squamous cell carcinoma (SCC). The proliferative activity is higher than that in typical SCC. However, BSC is also characterized by a high rate of apoptosis. Although prognosis of BSC does not differ significantly from that of typical SCC in early stages, advanced-stage BSC shows a poorer prognosis than typical SCC. Recent advances in molecular pathology have demonstrated peculiar features of BSC, including aneuploidy, frequent Bcl-2 expression, and less frequent expression of p16 protein. There is no doubt that BSC differs from typical SCC; however, further investigation is required to elucidate the detailed biological behavior of BSC.

Endocytoscopic observation of various esophageal lesions

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The “endocytoscopy system” (ECS), adapted for clinical use in 2003, is an ultra-high-power magnifying endoscope that allows observations at the cell level. Our group was the first to report *in vivo* observations of squamous epithelium and squamous cell carcinoma in the esophagus (2004) using first-generation ECS. ECS is based on the technology of light-contact microscopy. The most evident use of ECS is for real-time, high-resolution diagnosis of nuclear abnormalities, mainly in patients with esophageal cancer. Up to now, three ECS systems have been developed to solve the respective problems of each prototype. We have proposed “type classification” that classified ECS findings into three categories in tandem with iodine staining: Type 1, surface epithelial cells have a low nucleus/cytoplasm (N/C) ratio and a low cell density. No nuclear abnormality is evident; Type 2, there is a high nuclear density but no evident nuclear abnormality. No clear borders between cells are observed; Type 3, evidently increased nuclear density and nuclear abnormality, e.g. irregular nuclear size and shape, with hyperchromatism. In the normal esophageal mucosa, one or two layers of superficial cells with nuclei showing regular characteristics of staining, shape and dimension were evident. The nuclear-cytoplasmic ratio was low. Lower-magnification ECS of the cancerous region revealed a nuclear density much higher than that in the normal squamous epithelium. Using higher-magnification ECS, nuclear abnormality became evident.

Based on the 71 lesions of squamous cell carcinoma observed using both first- and second-generation ECS *in vivo*, we reported that it would have been justifiable for the pathologist to omit biopsy histology in 84% of cases observed using higher-magnification ECS, and in 66% of cases observed using lower-magnification ECS (2009). We concluded that higher-magnification ECS made it possible to omit biopsy histology in cases of squamous cell carcinoma.

Third-generation ECS can be used for screening examinations because this endoscope has almost the same diameter as that of conventional endoscopes currently on the market. Using this latest ECS, we investigated both neoplastic and non-neoplastic lesions of the esophagus, and clarified the features of their surface cell morphology (2012) **3)**. Although the diagnostic ability of the endoscopist, who was aware of the conventional endoscopic view, showed high sensitivity and specificity, that of the pathologist, who was blinded to the conventional endoscopic information, showed considerably low specificity. Then, we reported, by consultation with a pathologist, adequate magnification power of ECS (x600 on a 19-inch monitor) for recognition of nuclear abnormality (2014).

We will show the detailed characteristics of cell morphology observed by ECS for both neoplastic and non-neoplastic lesions.

Abstract 3

Barrett low grade dysplasia: a relevant finding or an innocent bystander?

Michael Vieth

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The histological diagnosis of low grade dysplasia in Barrett's esophagus seems to be difficult when searching the literature for diagnostic accuracy. It is still under debate whether low grade dysplasia is a relevant finding or just an innocent bystander that regresses for the most after an ill defined time interval.
The frequency of low grade dysplasia in Barrett's seems to have regional variances in consecutive series between 2-3% and 70%. The differences are so huge that one needs to note that all frequencies more than 5% are probably overdiagnoses of regenerative changes since esp. publications with high frequencies could show that there is no malignant progression even after a longer interval.
Even if it seems logical that we are dealing with overdiagnoses, it is stunning that the collegues are very consisting in reporting their "frequency". This means we are probably not dealing with real overdiagnoses due to lack of experience but the wrong criteria. And indeed, criteria how to diagnose dysplasia differ worldwide and there is no definitive proof whether one criteria is right or wrong and the definition of dysplasia comes back to the very basic definition given by Eduard Krompecher in Budapest in 1923: Dysplasia are abnormal cells under the microscope but are no cancer yet.
All our attempts to grade such dysplasia in low grade and high grade are just trying to estimate the risk for malignant progression but without clearly separating regenerative changes from truly neoplastic changes such grading will differ worldwide.
The best European data stem from Amsterdam and Bayreuth. Interestingly those groups show the same frequencies and the same aggressiveness in the recommendation for local treatment in Low grade dysplasia even if guidelines still recommend a more conservative watch and wait strategy.
But in conclusion it seems to be very clear that we are dealing with overdiagnoses in low grade dysplasia, and underdiagnosis of cancer in the Western World if a mixture of cytological and architecture criteria are used. A harmonization process is needed worldwide to allow comparision of different cohorts in the literature and estimate the personal risk for a certain patient more accurate to derive the best treatment option.

Abstract 4

Iatrogenic pathology of the upper gut

Professor Gregory Y. Lauwers
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Many drugs and chemical agents can cause esophagitis, gastritis and small bowel damages, producing a wide spectrum of clinical gastrointestinal side effects. The common symptoms vary from nausea and vomiting to abdominal pain while diarrhea and constipation can indicate a concurrent lower gastrointestinal tract involvement.

The histologic changes can be surprisingly broad from erosion, to acute inflammation, apoptosis and deposition of crystals.
Furthermore, significant histological overlap exists between some patterns of medication or chemical injury and various disease entities. In this lecture, pill esophagitis, esophagitis dissecans, proton pump inhibitors' effects, diaphragm disease will be reviewed. Also, the recently described effects of drugs such as olmesartan, mycophenolate, and of compounds such as yttrium-90 are to be discussed among several others. The inclusion of iatrogenic injury in the differential diagnosis of "conventional" diseases (such as gastric antral vascular ectasia, graft-versus-host disease) will be emphasized and pitfalls will be discussed. For example, a particular medication may cause multiple patterns of injury and may mimic common entities such as coeliac disease and others. Thus, given the frequent void of appropriate clinical information (e.g., a complete list of drugs taken by a patient) and the common absence of specific histopathological features, the diagnosis often relies upon thorough clinic-pathological correlation.

In conclusion, this lecture concentrates on selected examples of medication-induced injury of the foregut in which the pathology can be recognized, particularly on biopsies, with a focus on newly described medication-induced gastrointestinal effects. We underscore again the important and necessary communication between pathologist and clinician in the recognition of these entities to provide the best patient care.

Abstract 5

Handling Helicobacter Negative Gastritis

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Gastric biopsies are often taken to "rule out *H. pylori*. The biopsies may have changes that suggests that *Helicobacter* should be present, but special stains fail to detect the organism. It is useful to have an algorithm for dealing with these biopsies. This can be summarized as follows

1. Missed organisms - Was an appropriate special stain ordered? (just H&E is unreliable.)

False-negative stain. If a blue-on-blue stain (Cresyl violet, Giemsa, Diff-Quick, etc.) was carried out, do a silver, dual, or immunostain. Sometimes Helicobacter may only be present deep in the oxyntic mucosa, sometimes only within parietal cells, when either silver or immunostains are usually necessary to detect them.

2. Sampling. Are both antral and oxyntic mucosa present? If not, this could well be the reason as 10% to 15% of patients with *Helicobacter* have them in only one site (El-Zimaity, et al Can J Gastroenterol. 2013 Oct;27(10):e25-30). PPIs may also cause caudal migration of organisms so that they may only be found in oxyntic mucosa .

3. Assuming that acute inflammation is always present with Helicobacter. This is untrue, and some patients have only chronic inflammation, sometimes remarkably little. Some Helicobacter generate very little host response and one issue is whether they are really pathogenic at all.

4. Hostile environment

- Lack of acid. Helicobacter produce urease which results in a cloud of ammonium ions around the organism, requiring acid for its neutralization, as surprisingly, Helicobacter die at a pH >8, so lack of acid results in their death.

Does oxyntic mucosa have parietal mucosa with PPI changes. If oxyntic mucosa is present, are there hypertrophic parietal cells indicative of longterm PPI ingestion? PPIs can reduce *Helicobacter* to undetectable levels. Recent administration of PPIs however rapidly reduces numbers of *Helicobacter*, but the morphologic changes are not detectable on histology as it takes weeks for these changes to develop, so requires clinical input. Because PPIs may result in numerous organisms being able to grow in the stomach—both oral and duodenal, a *Helicobacter* immunostain is the stain of choice for determining if *Helicobacter* are present in and admixture of bacteria.

Is lymphocytic gastritis present? This is likely associated with marked reduction in acid secretion. In addition to the lamina propria infiltrate, and especially if this is active (neutrophilic), is there an intraepithelial lymphocytosis accompanied by marked (often just oxyntic) chronic active inflammation? If so, lymphocytic gastritis frequently has no *Helicobacter*, but serology is positive, and treatment with eradication therapy results in healing of the gastritis. This form of lymphocytic gastritis is usually easily distinguished from the mild intraepithelial lymphocytosis associated with celiac disease which is invariably only antral, focal and rarely has more than a mild chronic inflammatory infiltrate in the lamina

propria.

Is atrophic gastritis present? Atrophy with pseudopyloric metaplasia imitating antral mucosa without (or with minimal) intestinal metaplasia, is readily misinterpreted as antral mucosa. It is usually inflamed and because of lack of acid. *Helicobacter* are not found in either the residual antral or metaplastic mucosa. However, to recognize this requires the ability to distinguish antral mucosa from oxyntic mucosa that has undergone complete atrophy with pseudopyloric metaplasia. If all biopsies appear to be antral (nonoxyntic), a hint to help identify pseudopyloric metaplasia is that one needs to evaluate if all biopsies are similar regarding inflammation and architecture. If different (e.g., one/some are inflamed or architecturally different— especially loss of glands [atrophy] and one/some are noninflamed or with regular architecture), the likelihood is that the inflamed biopsies, which invariably have a degree of gland loss, represent oxyntic mucosa with atrophy and pseudopyloric metaplasia. An immunostain for gastrin will show the antral biopsies by the presence of G cells, while their lack indicates atrophic oxyntic mucosa. If gastrin stain is not available, then chromogranin A or synaptophysin immunostain can serve a similar function, but now the distribution of endocrine cells needs to be evaluated. G cells primarily form a band below the mucous neck, with few or no cells in the pyloric glands. Conversely oxyntic mucosa has regularly spaced endocrine cells if normal, but with long-standing hypergasrtinemia resulting in their hyperplasia, these form chains (linear hyperplasia) and small clusters of endocrine cells (microcarcinoids), and they also migrate to the base of the crypt close to the muscularis mucosae. In some patients, these changes are detectable on H&E stain as the crypt bases can develop a double layer of nuclei, the outer layer being the endocrine cells.

Intestinal metaplasia. *Helicobacter* will not grow in intestinal type mucosa whether native or metaplastic. So if, for example, two antral biopsies are taken and both are completely metaplastic, no organisms may be detected. Unless the proximal mucosa is also sampled, the organisms will not be found.

Diffuse reactive gastropathy (medications, post-surgical). . Organisms are rarely found in the absence of mucin, so when there is diffuse reactive (chemical – such as with NSAIDs, ASA, antiplatelet medications, bisphosphonates) gastropathy, *Helicobacter* are rarely found. The same is true of patients post–gastric resection or gastroenterostomy, there is pathologic duodenogastric reflux with resulting diffuse gastropathy. Even if *Helicobacter* are present proximally, marked mucin depletion can prevent their identification in the part of the stomach affected by reflux.

4. Other infections. These include CMV, syphilis, and other bacteria (*Micrococcus*). Immunostains to CMV if not visible on the H&E sections and *Treponema pallidum* (together with good clinical suspicion) are required for these to be considered.

5. Recent administration of antibiotics or Helicobacter eradication therapy.(This clearly needs clinical input.

The chronic inflammation following *Helicobacter* eradication can take months and sometimes over a year to completely subside. It is likely that rare instances of spontaneous eradication occur, or that eradication occurs when patients are put on antibiotics or other reasons. Either way, the chronic inflammation persists for a time.

6. **An up-regulated immune system**—IBD, especially Crohn's disease, in which a modest diffuse chronic superficial inflammation is often present, but also ulcerative colitis can cause this, invariably when there is active large bowel disease and pediatric population. Appropriate clinical input is required

for this. However other “autoimmune” disorders can also result in a superficial gastritis

7. Idiopathic gastritis. If the above have been excluded, there remains a group of patients in whom there appears to be no known cause despite extensive investigation. Pathologists seeing gastric biopsies regularly are well aware of this subgroup as it is not small and may account for perhaps 15% to 25% of biopsies. It therefore has to be acknowledged that there are a group of patients with chronic (less commonly chronic active) gastritis with no known cause. Fortunately, most of the gastritis is relatively mild and is *Helicobacter* negative in multiple biopsies and serologically. These are signed out simply as “chronic gastritis; *Helicobacter* are not identified”. However, this diagnosis should not be used casually and until all other identifiable causes of inflammation resembling *Helicobacter* have been excluded as outlined above. This group of patients have a modest gastritis that changes little with age.

Abstract 6

Do the different definitions of Barrett's esophagus destroy friendships, or can friends overcome these differences?

Henry Appelman, M.D.

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Barrett's mucosa is a metaplastic columnar mucosa that presumably replaces normal squamous mucosa in the distal esophagus, extending proximally for various distances. It is thought to result from chronic gastroesophageal reflux. Its importance is that it is a precursor for adenocarcinoma which may develops in a precursor known as dysplasia. This metaplastic mucosa is most easily recognized when it contains goblet cells, that is, when it is intestinalized, because goblet cells in this area are clear evidence of metaplasia, intestinal metaplasia (IM). It has been postulated that only IM mucosa has a carcinoma association. However, columnar mucosa that is not intestinalized (non-IM) and that is similar to cardiac mucosa of the most proximal stomach is occasionally found lining the distal esophagus. No one knows for certain if non-IM mucosa is also metaplastic or if it is a normal variant. In some parts of the world, this non-IM mucosa lining the distal esophagus is thought to be part of the Barrett's spectrum, and that it also has a cancer association. There are studies indicating that in about a third of the time, this Non-IM mucosa contains intranuclear CDX2, an intestinal differentiation marker, even though it has no goblet cells. In some studies, this non-IM mucosa more commonly surrounds small adenocarcinomas and dysplasias in the distal esophagus than does IM mucosa. Other studies dispute this and present evidence that the cancer risk for non-IM distal esophageal mucosa is miniscule compared to IM mucosa. Data such as this have led to opposing views as to the importance of the non-IM cardiac type mucosa, and whether it should be included as a cancer prone mucosa, comparable to that with goblet cells. These opposing views have led in turn to heated disagreements among friends in the esophageal pathology community over whether goblet cells should be required for the diagnosis of Barrett's mucosa. Is this disagreement enough to end long standing friendships? This presentation will deal with this in depth.

The education of a young pathologist: A professional debt of gratitude to influential pathologists and clinicians

Kaiyo Takubo, MD, PhD

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I graduated from Nippon Medical School in 1975. For 5 years thereafter, I was belonged in two departments: the Department of Surgery at Nippon Medical School, and the Department of Pathology at Saitama Cancer Center Research Institute. In 1976, *Dr Yoshio Mitomo*, the Director of the Department of Pathology at Saitama Cancer Center Research Institute, strongly recommended me to study esophageal pathology, because the incidence of esophageal carcinoma was high in Saitama prefecture. He taught me for only 2.5 years. Thereafter, I performed about 500 autopsies within a period of about 15 years, carrying out histological examinations of esophageal samples with reference to the descriptions in cover papers by *Drs Yoichi Tanaka and Ken-ichi Mafune*.
In 1985, when I was 35 years old, *Dr Takeo Nagayo*, President of Aichi Cancer Center, invited me to become a member of the committee of the Pathological Classification of Esophageal Carcinoma of the Japanese Research Society for Esophageal Carcinoma (now JES). *Prof Wang Quan-hong* also invited me as a keynote speaker to the International Symposium at Zhuhai city. I was also taught the methodology for comparison between endoscopic and pathologic findings by *Drs Misao Yoshida, Miwako Arima, Takayuki Nishi, Osamu Chino, and Tsuneo Oyama and Profs Hiroyasu Makuuchi and Teruo Kozu*.
In 1991, I was invited to transfer to the Tokyo Metropolitan Geriatric Hospital, which later became the Institute of Gerontology, by Dr Yukiyoshi Esaki. In 1995, I studied Barrett's esophagus at the Departments of Pathology of Auckland University School of Medicine and Auckland Hospital, where the directors were *Prof Jeremy Jass and Dr Johanna Nixon*, respectively. I was fortunate to meet some very good teachers among the reviewers I encountered in the process of submitting papers for publication. They taught me how to write a good scientific paper through my submissions. These reviewers, who I believe were *Profs Henley Appelman and Robert Riddell*, taught me to include the itemized main findings in the first part of the Discussion section, and then to discuss each of these findings in turn.
In 2006, I was given many paraffin blocks of EMR specimens containing Barrett's carcinoma (BC) by *Prof Michael Vieth* (141 cases), and we used these blocks for research. He and I discussed the histogenesis of BC, in which small BCs are surrounded mainly by cardiac-type mucosa. I am now discussing the definition of Barrett's esophagus with *Profs Gregory Lauwers, Riddell, Appelman, and Vieth*. I have written several papers on palisade

veins with *Drs Yoshio Hoshihara, Youichi Kumagai, and Junko Aida, and Prof Katsuhiko Iwakiri.* We defined palisade veins as veins >100 μm in diameter located within the mucosa. I have also cooperated with *Dr Kumagai* to write many papers on endocytoscopy, and discussed the histologic criteria for high-grade dysplasia and BC with *Profs Lauwers, Riddell, Appelman, and Vieth and Drs Tomio Arai and Aida.*

I have thus been educated by many pathologists and clinicians, and published more than 300 papers in English. As a medical researcher for 40 years, I have always considered that my articles are constantly improving in quality, which means that my best and most representative paper will always be the next one!

Abstract 8

History of Japanese Society for Esophageal Diseases and Japan Esophageal Society

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Japanese Society for Esophageal Diseases (JSED) was organized in 1965 in order to promote surgical treatment of esophageal cancer. JSED made the guidelines for the clinical and pathologic studies on carcinoma of the esophagus that allowed us to describe esophageal cancer cases and to organize the comprehensive registry of esophageal cancer. Annual meetings of JSED and the registration system revealed tasks in clinical and research activities. JSED improved surgical results of esophageal cancer such as five-year survival rate from 12% (1968) to 52% (2008), and operative death rate from 10% (1968) to 2.3% (2008). Another achievement of JSED is the developments in the field of superficial cancer of the esophagus. Endoscopic staining realized detection of mucosal cancer, and revealed that mucosal cancer seldom had lymph node metastasis. Endoscopic treatments (EMR/ESD) realized the esophagus preserving treatments of esophageal cancer. The Japan Esophageal Society (JES) succeeded objectives and activities of JSED in 2003. JES established the official journal “ESOPHAGUS” in English. It encouraged many specialists such as pathologists gastroenterologists, radiologists, endoscopists, oncologists and surgeons join in studies on esophageal diseases not only esophageal cancer but also benign diseases, and announce results of their studies abroad earlier than before. JES also published the guidelines for treatment of esophageal cancer to give doctors and patients suggestion of standard treatments for esophageal cancer including endoscopic treatments, surgery, radio-chemotherapy and others.