The Hong Kong Society of Gastroenterology
香 港 腸 胃 學 會

December
2019

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President Message

Welcome to our December 2019 Newsletter!

In 2019, The Hong Kong Society of Gastroenterology has seen a stable year with scientific meetings organized in March and September, although the 21st Joint Annual Scientific Meeting scheduled in September was finally cancelled due to unstable circumstances in Hong Kong. Our Society also continued supporting the Medical Multispecialty Mega Conference and the IDD Forum. Two newsletters were published in the year. Research grants were allocated for 2 research projects to be completed in 2 years.

On behalf of the Society, I wish to express my gratitude to all who have contributed to the Society: Dr. Wai-Fan Luk for organizing the Annual General Meeting cum Scientific Meeting 2019, Professor Justin Wu for organizing the 21st Joint Annual Scientific Meeting, Professor Wai-Keung Leung for editing the two newsletters, Professor Jan Tack and Dr. Carly Sun for their scientific updates in this newsletter. Last but not least, all the sponsors who rendered support and contributions to the Society throughout the year.

The next newsletter will be published in June 2020.

Best wishes for a merry Christmas and a happy new year.

Dr. Annie O.O. Chan
President, The Hong Kong Society of Gastroenterology

Scientific Updates

From Guidelines to Clinical Practice: Irritable Bowel Syndrome

Professor Jan Tack
Head of Clinic, Gastroenterology Division
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A number of guidelines for the diagnosis and management of irritable bowel syndrome (IBS) have been issued by various international societies, but these guidelines are complicated and challenging to apply in clinical practice. Furthermore, these guidelines are not well known or used by primary care physicians.[1,2] Therefore, Professor Tack applies a diagnostic algorithm in routine clinical practice that represents a composite of various guidelines comprising:

1. Clinical history (+ criteria)
2. Physical examination
3. Laboratory tests
4. Colonoscopy or other tests (if indicated)

Diagnosing IBS

When assessing patients, Professor Tack looks for abdominal pain/discomfort and bloating/distension that is relieved by defaecation or associated with altered bowel function.[3] While a clinical examination may suggest IBS, laboratory testing is required to rule out alarm features because the symptoms of IBS are non-specific and overlap with organic disease. Alarm features include[4]:

- Age ≥50 years old (or local colon cancer risk age threshold)
- Blood in stools
- Nocturnal symptoms
- Unintentional weight loss
- Change in symptoms
- Recent antibiotic intake
- Family history of organic gastrointestinal disease (e.g. inflammatory bowel disease, cancer, coeliac disease)

Laboratory tests should include a full blood count and tests for inflammatory markers, such as C-reactive protein and erythrocyte sedimentation rate.[4] Thyroid function may also be investigated in patients with extremes of stool patterns (i.e. severe diarrhoea or constipation). If no abnormality is detected, then the condition should be managed as IBS. Otherwise, any organic disease should be treated as indicated.

First-line treatments for IBS

The efficacy of a number of inexpensive first-line therapies for IBS has been confirmed in meta-analyses.[5-7]

Diet

An altered diet can relieve the symptoms of IBS, but can be complicated and require referral to a dietician to help eliminate fermentable oligo-, di- and monosaccharides, as well as polyols.[8] Fibre can also relieve constipation.[7] However, in Professor Tack's experience, dietary modification is only efficacious in 30–35% of patients and the most appropriate place for diet in the IBS treatment algorithm remains unclear.

Laxatives

Laxatives increase the number of bowel movements, but do not improve abdominal pain, bloating and discomfort.[9]

Antidiarrhoeal agents

Antidiarrhoeal agents, such as loperamide, are efficacious and suitable for chronic administration at a titrated dose, but do not relieve abdominal pain or bloating.[7]

Significantly more patients administered eluxadoline, a μ opioid receptor agonist and δ/κ opioid receptor antagonist, also respond to treatment compared with placebo, although there is no significant benefit for abdominal pain symptoms.[10] However, eluxadoline is associated with an increased risk of pancreatitis and sphincter of Oddi spasm, and is contradicted in several patient populations, including patients who have undergone cholecystectomy, severe hepatic impairment or a history of alcohol use disorder.[10,11]

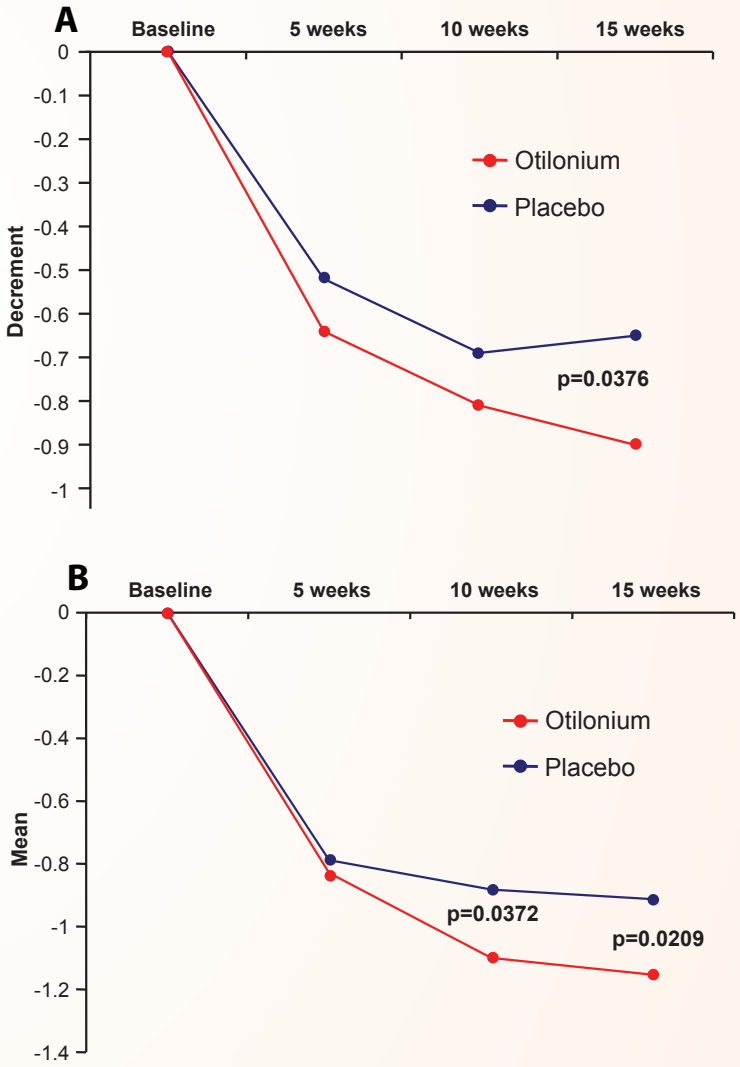
Antispasmodics

Antispasmodics have a significant effect on abdominal pain.[5,6] In particular, a greater distending pressure is required before patients treated with otilonium bromide experience abdominal pain and the maximum tolerable pressure is higher versus placebo, but a significant improvement versus placebo was not observed until 15 weeks in the OBIS study **(Figure 1A)**.[12,13] However, a significant decrease in the severity of bloating was observed after 10 weeks and the proportion of patients discontinuing due to relapse was significantly lower than placebo **(Figure 1B)**.[13] Otilonium bromide is also well-tolerated and the long duration of action of otilonium bromide means that the average time to relapse is significantly longer than placebo after ceasing treatment.[13] Peppermint oil may also be efficacious, but is associated with peppermint-tasting reflux.[5,6]

Probiotics

Probiotics are recommended for patients with IBS, but it is not clear which probiotic should be used, for how long and for which patients.[6]

Figure 1 (A) Frequency of pain and **(B)** intensity of bloating during treatment with otilonium bromide in the OBIS study (intention-to-treat population)[12,13]



Second-line treatments for IBS

Constipation-predominant IBS (IBS-C)

Lubiprostone is associated with a significantly increased response rate versus placebo.[14] Likewise, the guanylyl cyclase inhibitor linactolide has a responder rate 18–23% higher than placebo at 12 weeks, but is more expensive and increases the risk of diarrhoea.[15]

Diarrhoea-predominant IBS (IBS-D)

Alosetron is not available in Europe. Antagonists of the 5-hydroxytryptamine 3 (5-HT_3) receptor like ondansetron can improve stool consistency for patients with the diarrhoeal subtype of IBS, but do not affect abdominal pain intensity or bloating severity.[16] Furthermore, approximately 25% of patients with IBS-D have high levels of bile acids in their stool and may benefit from cholestyramine therapy.[17]

Abdominal pain
Tricyclic antidepressants and selective serotonin reuptake inhibitors can be efficacious for relieving abdominal pain in patients with IBS.[18] The antibiotic rifaximin is also effective in reducing abdominal pain, but is perhaps best left as an option for patients where there is evidence of bacterial overload because of its broad-spectrum action, which may negatively affect the overall health of the gut microbiota.[19]

Conclusions
The presence of typical symptoms, the absence of alarm features, alongside laboratory tests and examinations may be used to diagnose IBS.[4] Spasmolytics, antidiarrhoeal agents and anti-constipation therapies are all first-line treatment options, but the OBIS trial indicated that otilonium bromide has the added benefit of reducing the frequency of abdominal pain and severity of abdominal bloating compared with placebo.[5-7,13] Furthermore, otilonium bromide is well-tolerated and has a long duration of action.[13] Second-line treatment options target the symptoms of subtypes of IBS such as diarrhoea or constipation, while neuromodulators may be used to treat IBS-related pain.

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Diagnostic Yield and Clinical Impact of Capsule Endoscopy on Management of Patients with Suspected Small Bowel Bleeding (Summary of Thesis 2018)

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Introduction
Small bowel bleeding refers to bleeding from a source distal to the major duodenal papilla and proximal to the ileocecal valve, and accounts for approximately 5% of gastrointestinal bleeding.[1-3] Patients with small bowel bleeding underwent more diagnostic procedures, had higher transfusion requirement, longer hospital stay, and higher cost of hospitalization, when compared with those who had bleeding from other gastrointestinal sources.[4] Small bowel capsule endoscopy (CE) was recommended as the first-line investigation for evaluation of small bowel bleeding source in hemodynamically stable patients after negative oesophago-gastro-duodenoscopy (OGD) and colonoscopy.[1-3]

The primary objective of this study was to determine the diagnostic yield of small bowel CE in identifying the source of bleeding in patients with suspected small bowel bleeding. Secondary objectives were to investigate the impact of CE on clinical management, rebleeding rates, and clinical factors associated with positive findings on CE.

Methods
Study design
This was a retrospective study of patients aged ≥18 years who underwent CE for investigation of suspected small bowel bleeding at Pamela Youde Nethersole Eastern Hospital (PYNEH) between July 2007 and December 2016. Before CE, all patients underwent at least one complete OGD and colonoscopy without bleeding source identified. EndoCapsule® EC-1 (Olympus), PillCam®SB2 or PillCam®SB3 (Given Imaging) was used.

Small bowel bleeding was classified into overt and occult types. Overt bleeding was defined as the presence of melena or hematochezia, and sub-classified into ongoing-overt (presence of melena or hematochezia during CE) and previous-overt bleeding (CE performed after the last episode of overt bleeding). Occult bleeding was defined as unexplained iron-deficiency anemia ± positive fecal occult blood tests.[1]

CE examination was positive if clinically significant finding was present, including angiodysplasias, ulcerations, multiple erosions, tumours, active bleeding without identifiable source, and bleeding sources in upper gastrointestinal tract/colon that were not documented in prior endoscopies. Red dots, isolated erosion or polyp were clinically insignificant. The diagnostic yield of CE was defined as the rate of detection of clinically significant lesions that could account for gastrointestinal bleeding. Rebleeding was defined as bleeding from suspected small bowel sources, as evidenced by passing melena or hematochezia ≥30 days after the index bleeding episode, or unexplained drop of hemoglobin level by >2g/dL ≥30 days post-CE. Re-evaluation was arranged to determine the source of bleeding unless contraindicated or patient refusal. For rebleeding analysis, patients were excluded if follow-up <12 months and did not develop rebleeding. Rebleeding from small bowel or sources that remained obscure despite repeated investigations were included; bleeding from non-small bowel sources were excluded.

Statistical analysis

Statistical analysis was performed using SPSS version 22.0 for Windows. Categorical data were expressed as frequency and percentage, and compared between groups by Chi-square test or Fisher's exact test. Continuous variables were expressed as mean ± standard deviation (SD) and compared by Student's t-test, or median and interquartile range (IQR) and compared by Mann-Whitney U test if normal distribution was not present. Factors which approached significance ($p<0.1$) in univariate analysis were included in multivariate analysis. Binary logistic regression was performed to identify independent factors associated with positive CE examination. A two-sided p-value of <0.05 was regarded as statistically significant.

Results

During the study period, 334 patients were included in the analysis **(Figure 1)**. The mean age was 64.9±16.0 years. 18 (5.4%) patients had ongoing-overt bleeding, 155 (46.4%) had previous-overt bleeding and 161 (48.2%) patients had iron-deficiency anemia. The median time interval between index overt bleeding episode and CE examination date was 32 days (IQR 14-69 days). Median small bowel transit time was 120 minutes (IQR 68-224 minutes). There was no significant difference in detection rates of the three capsule models. Three (0.9%) patients developed capsule retention.

CE findings and subsequent management

The diagnostic yield of small bowel CE was 40.4%, with 120 (88.9%) small bowel lesions and 15 (11.1%) lesions within reach of OGD/colonoscopy but unidentified on initial endoscopies **(Figure 2)**. Patients with overt bleeding had similar diagnostic yield compared with occult presentation (42.8% vs. 37.9%, p=0.36). The diagnostic yield for ongoing-overt bleeding was significantly higher than other forms of presentation (83.3% vs. 38.0%, $p<0.001$). Fifty-one patients had small bowel angiodysplasia (47 directly visualized on CE; 4 had fresh blood only). Forty-seven patients had small bowel ulcerations/multiple erosions, and subsequent clinical diagnoses included aspirin/NSAID-induced enteropathy (23), Crohn's disease (6), vasculitis with small bowel involvement (3), and undetermined etiologies (15). Twenty-two patients had active bleeding without visualized lesions on CE, and subsequent investigations revealed underlying pathology in half, with the majority being small bowel angiodysplasia and tumours. Seven small bowel tumours were diagnosed post-CE (direct tumour visualization in 3; fresh blood detected in 4). However, CE failed to identify two other patients with duodenal gastrointestinal stromal tumours, which were only diagnosed by CT-enterography after rebleeding occurred. Seventy-two patients received specific treatment post-CE, with 19 receiving endoscopies for hemostasis and 14 receiving surgery. Medication was modified in 47 patients, including addition of Misoprostol/ immunosuppressant/ proton pump inhibitors, or discontinuation of antiplatelet drugs/ anticoagulants/ NSAIDs.

Rebleeding

After excluding 42 patients with follow-up period of <12 months and who did not develop rebleeding, 292 patients were included in rebleeding analysis, with median follow-up period of 50 months (IQR 27-77 months). The overall and one-year rebleeding rates were 20.5% and 11.3%, respectively. Overall, rebleeding from small bowel/obscure sources developed in 60 (20.5%) patients, while 30 (10.3%) other patients developed bleeding from non-small bowel sources. Both overall and one-year rebleeding rates of patients with negative CE were significantly lower than that of patients with positive CE.

Factors associated with positive CE findings

On multivariate analysis, ongoing-overt bleeding (OR 9.70, 95% CI 2.16-43.58, p=0.003), and more frequent hospital admissions related to gastrointestinal bleeding (OR 1.39, 95% CI 1.03-1.87, p=0.034) were independently associated with positive CE examination.

Figure 1. Study recruitment and participant flow.

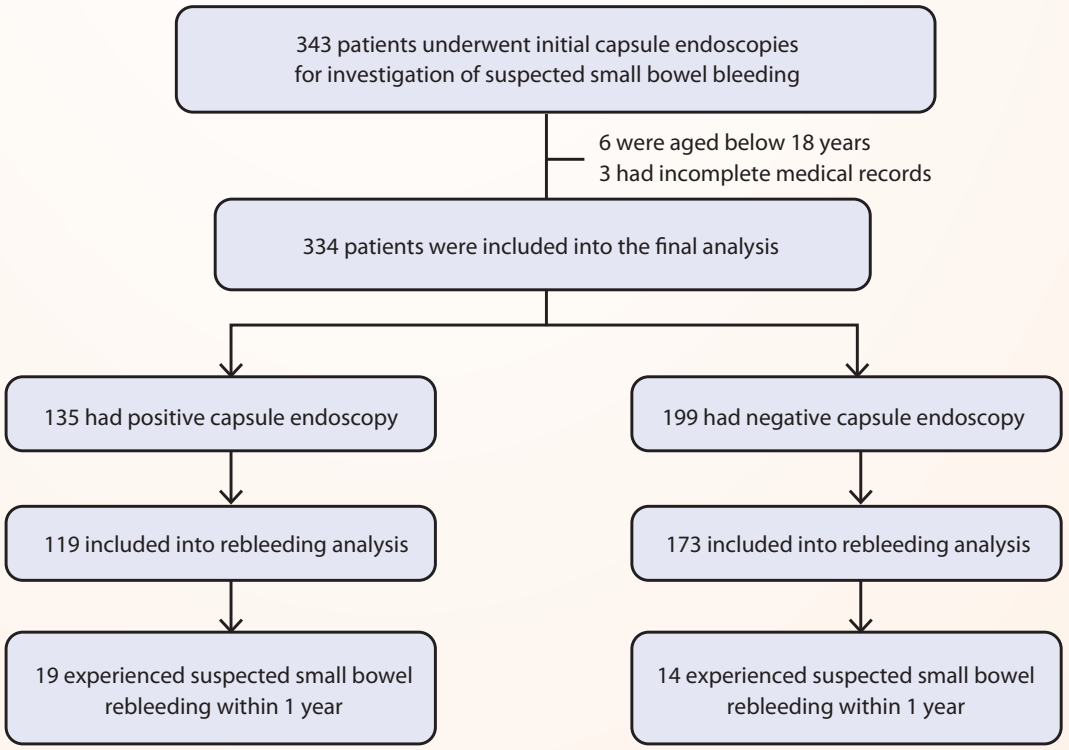
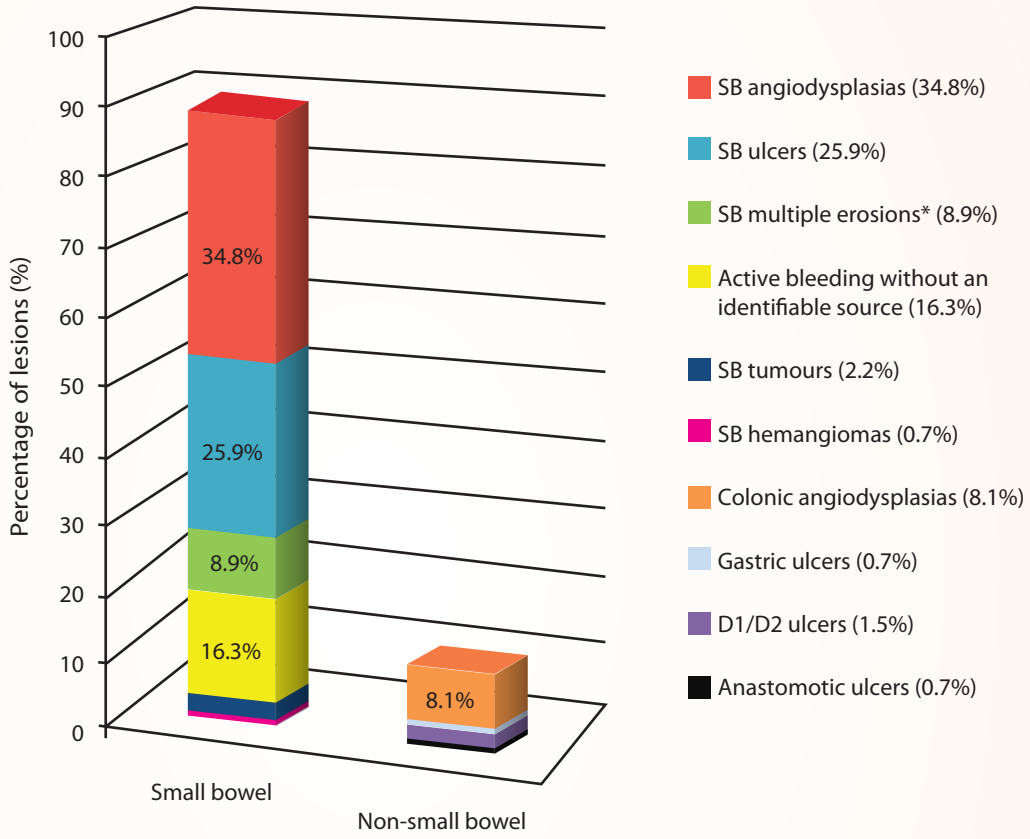


Figure 2. Significant capsule endoscopy findings (n=135)



*Defined as presence of >3 erosions
SB, small bowel; D1/D2, first or second part of duodenum

Discussion

The diagnostic yield of CE in our study was 40.4%, while published studies reported 30% to 64%.[5-7] The diagnostic yield in two local studies that recruited only patients with overt-obscure gastrointestinal bleeding was 53.3% and 63.3%, respectively; patients either underwent CE during the same hospital admission or immediately after non-diagnostic OGD and colonoscopy.[5,6] The lower detection rate in our study was accountable by the large variation of time interval between index bleeding episode and date of CE examination (median duration of 32 days) and that the majority (70.5%) of patients with overt bleeding underwent CE after 14 days. If we analyse the subgroup of patients with overt bleeding and CE performed within 14 days of index bleeding episode, the diagnostic yield would increase to 47.1%. Early CE after non-diagnostic OGD and colonoscopy should be considered to improve detection rates.

Most studies reported the long-term outcome of patients undergoing CE in terms of rebleeding rates, ranging from 17% to 33%.[5,6,8] The variation could be due to different definitions of rebleeding, follow-up duration and management. The relatively low rebleeding rate in our study could be due to the exclusion of bleeding episodes from confirmed non-small bowel sources. We found that 10.3% of patients who developed melena/hematochezia or hemoglobin drop of >2g/dL post-CE, had bleeding sources elsewhere in the upper gastrointestinal tract/colon. Thus, repeating OGD or colonoscopy should be considered before repeating small bowel examination. When analysing patients with negative CE only, 58.3% of rebleeding occurred within one year post-CE. Since substantial proportion of patients developed rebleeding after one year, the follow-up period should be extended beyond one year post-CE even for patients with negative CE. The one-year rebleeding rate was highest (31.6%) in patients with CE finding of active bleeding without identifiable source. Further investigations should be performed and those whose underlying bleeding source remain obscure require close monitoring for any rebleeding, as clinically significant lesions were subsequently detected including 4 small bowel tumours.

Positive CE examination altered clinical management in half of our patients who received specific treatment as a result of detection of clinically significant findings. CE can aid the selection of enteroscopy by estimating the location of small bowel lesion. Despite the inability to make definitive diagnosis, negative CE still has clinical implication on subsequent management. A meta-analysis that included 26 studies with 3657 patients concluded that patients with negative CE had low risk of rebleeding.[9] Some guidelines and studies suggested that these patients can be closely observed until rebleeding occur, instead of undergoing further extensive investigations.[2,3,6,8] Our finding of low rebleeding rates after negative CE examination also support this management approach.

Our study limitations include retrospective design and non-standardized patient management. There was potential selection bias (as CE was self-financed) and inter-observer discrepancy in the interpretation of CE findings. Nonetheless, all CE findings were reported by experienced gastroenterologists, and images were reviewed again during data collection.

Conclusion

CE was a practical and non-invasive investigation for patients with suspected small bowel bleeding, with a modest diagnostic yield for clinically significant findings. CE had a clinical impact and altered subsequent management in more than half of the patients with positive examination.

Acknowledgement

I would like to thank the Gastroenterology and Hepatology team, Department of Medicine, PYNEH, for their support and guidance.

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Welcome! New Members

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Departmenr of Medicine and Geriatrics
Princess of Margaret Hospital
Hong Kong

Dr. Carla Pui-Mei LAM
Department of Medicine
Queen Mary Hospital
Hong Kong

Dr. Kin-Kit LAW
Department of Medicine and Geriatrics
Caritas Medical Centre
Hong Kong

Coming Soon

The Hong Kong Society of Gastroenterology
39th Annual General Meeting cum Scientific Meeting
Thursday, 19 March 2020 6:15 pm

Venue: Level 7, Cordis Hong Kong at Langham Place
555 Shanghai Street, Mongkok, Kowloon

Organizing Chairperson: Dr. Wai-Fan Luk

Presentation of Honorary Fellowship by President, Dr. Annie O.O. Chan

Surveillance of gastric intestinal metaplasia finally coming of age

Professor Ernst J. Kuipers
Professor of Medicine
Department of Gastroenterology & Hepatology
Erasmus University Medical Centre
Rotterdam, The Netherlands

Case Presentation: Double-balloon enteroscopy assisted ERCP for patients with surgically altered anatomy

Dr. Ka-Shing Cheng
Associate Consultant
Department of Medicine
Tuen Mun Hospital
Hong Kong

Annual General Meeting

(More information will be available soon from www.hksge.org)

Major Meetings

3-5 December 2019
34th International Workshop on Therapeutic Endoscopy
Organizers: CUHK Institute of Digestive Disease,
CUHK The Nethersole School of Nursing,
Hong Kong Society of Digestive Endoscopy and
CUHK Jockey Club Minimally Invasive Surgical Skills Centre
Location: Prince of Wales Hospital, Hong Kong
Website: www.hksde.org/workshop.htm

12-15 December 2019
Asian Pacific Digestive Week (APDW 2019)
Organizers: Asian Pacific Digestive Week Federation (APDWF),
Asia Pacific Association of Gastroenterology (APAGE),
Asia Pacific Association for the Study of the Liver (APASL),
Asian Pacific Society for Digestive Endoscopy (A-PSDE) and
ISDS Asian Pacific
Location: Kolkata, India
Website: www.apdw2019.com/

14 December 2019
Symposium 2019 of State Key Laboratory of Liver Research (HKU) and Theme-based Research Scheme Project on Liver Cancer Stemness
Organizers: State Key Laboratory of Liver Research (HKU),
Department of Pathology of LKS Faculty of Medicine HKU and
Theme-based Research Scheme Project on Liver Cancer Stemness of UGC
Location: The Park Lane Hong Kong Hotel, Hong Kong
Website: www.skllr.hku.hk/News-And-Events/Events

12-15 February 2020
15TH Congress of European Crohn's and Colitis Organisation (ECCO 2020)
Organizer: European Crohn's and Colitis Organisation
Location: Vienna, Austria
Website: www.ecco-ibd.eu/ecco20.html

13-14 February 2020
Primary Liver Cancer – Emerging Concepts and Novel Treatments
Organizer: Falk Foundation e.V.
Location: Mainz, Germany
Website:
falk-foundation-symposia.org/uploads/tx_tocfpshoperw/Workshop_Mainz_2020_Preliminary_Program_01.pdf

20-22 February 2020
10th Biennial Congress of ASEAN Society of Colorectal Surgeons
Organizer: ASEAN Society of Colorectal Surgeons (ASCS)
Location: Bangkok, Thailand
Website: http://ascs2020.org/

28 February – 1 March 2020
Canadian Digestive Diseases Week (CDDW 2020)
Organizers: Canadian Association of Gastroenterology
Location: Quebec, Canada
Website: www.cag-acg.org/cddw

4-8 March 2020
29th Annual Conference - Asian Pacific Association for the Study of the Liver (APASL 2020)
Organizer: The Asian Pacific Association for the Study of the Liver
Location: Bali, Indonesia
Website: www.apasl2020.org/

5-8 March, 2020
Americas Hepato-Pancreato-Billiary Association 2020 Annual Meeting
Organizer: Americas Hepato-Pancreato-Billiary Association (AHPBA)
Location: Florida, USA
Website: www.ahpba.org/annual-meeting/

7-10 March 2020
ENDO 2020 – 2nd World Congress of GI Endoscopy
Organizer: World Endoscopy Organization
Location: Rio de Janeiro, Brazil
Website: http://endo2020.org/

19 March 2020
39th Annual General Meeting cum Scientific Meeting of The Hong Kong Society of Gastroenterology
Organizer: The Hong Kong Society of Gastroenterology
Location: Cordis, Hong Kong at Langham Place, Hong Kong
Website: www.hksge.org

25-27 March 2020
13th Annual Sydney International Endoscopy Symposium (SIES)
Host: Westmead Hospital, Sydney
Location: Sydney, Australia
Website: http://www.sies.org.au/

25-28 March 2020
FNM 2020 4th Meeting of the Federation of Neurogastroenterology & Motility
Organizer: Federation of Neurogastroenterology & Motility
Hosted by: Australasian Neurogastroenterology and Motility Association
Location: Adelaide, Australia
Website: http://fnm2020.org.au/

9-11 April 2020
Korea International Gastric Cancer Week 2020 (KINGCA Week 2020)
Organizer: Korean Gastric Cancer Association
Location: Seoul, Korea
Website: www.kingca.org/html/

15-19 April 2020
EASL - The International Liver Congress 2020
Organizer: European Association for the Study of the Liver
Location: London, United Kingdom
Website:
http://easl.eu/event/the-international-liver-congress-2020/

23-25 April 2020
ESGE Days 2020
Host: European Society of Gastrointestinal Endoscopy (ESGE)
Location: Dublin, Ireland
Website: http://esgedays.org/

2-5 May 2020
Digestive Disease Week (DDW 2020)
Organizers: American Association for the Study of Liver Diseases (AASLD), American Gastroenterology, Association (AGA),
American Society for Gastrointestinal Endoscopy (ASGE) and
The Society for Surgery of the Alimentary Tract (SSAT)
Location: Chicago, USA
Website: www.ddw.org/home

8-10 May 2020
Tokyo International Endoscopy Live Seminar 2020
Location: Tokyo, Japan
Website: www.coac.jp/tokyolive/english/

18-20 June 2020
The 8th Annual Meeting of the Asian Organization for Crohn's & Colitis (AOCC 2020)
Organizer: Asian Organization for Crohn's & Colitis
Host: The Korean Association for the Study of Intestinal Diseases
Location: Busan, Korea
Website: http://aocc2020.org/

10-14 October 2020
28th UEG Week
Organizer: United European Gastroenterology (UEG)
Location: Amsterdam, The Netherlands
Website: www.ueg.eu

(More information is available from www.hksge.org)

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