The 33rd Annual Assembly of General Surgeons

An Annual Celebration of General Surgery Training and Research

May 27, 2010
The Sutton Place Hotel
955 Bay Street
Toronto, Ontario

2010
E. Bruce Tovee Invited Lecturer
Murray F. Brennan, MD. FACS.
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<th>Year</th>
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<td>2010</td>
<td>Murray F. Brennan</td>
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The 33rd Annual Assembly of General Surgeons

An Annual Celebration of General Surgery Training and Research

Featuring:

Research Presentations and Posters

The E. Bruce Tovee Invited Lecturer - Dr. Murray F. Brennan

The State of the Union Address

Presentation of the Robert Mustard Mentorship Award

Annual Assembly Research Awards

Introduction of the 2010 Graduates of General Surgery

The Valedictory Address
PROGRAM

London Suite – 2nd Floor
7:00 – 8:00 CLOSED SESSION BY INVITATION ONLY

General Surgery Fellows Symposium
With Dr. Murray F. Brennan
Chair: Dr. Robert Tasevski - Chief Administrative Fellow

Queen Victoria Foyer (2nd Floor)

7:30 General Registration
With Continental Breakfast

Queen Victoria Ballroom (2nd Floor)

8:15 Welcome
Dr. Andrew J. Smith
The Bernard & Ryna Langer Chair
Division of General Surgery

Dr. Richard Reznick
R.S. McLaughlin Professor and Chair
Department of Surgery

8:30 Paper Session I
Chair: Dr. Rebecca Gladdy

Queen Victoria Foyer (2nd Floor)

9:15 Poster Session I and Break
Dr. Nancy Baxter

Queen Victoria Ballroom (2nd Floor)

9:45 Paper Session II
Chair: Dr. Teodor Grantcharov

Queen Victoria Foyer (2nd Floor)

10:45 Poster Session II and Break
Dr. Avery Nathens

Queen Victoria Ballroom (2nd Floor)

11:15 Introduction of the Bruce Tovee Lecturer
Drs. Bryce Taylor and Carol Swallow

“Lessons Learned From Mentor to Deuteronomy”
Dr. Murray F. Brennan
Vice President for International Programs
Benno C. Schmidt Chair in Clinical Oncology
Memorial Sloan-Kettering Cancer Centre
New York, NY
**PROGRAM**

**Lunch**
Stop 33
33rd Floor
12:30

Queen Victoria Ballroom (2nd Floor)

**Symposium on Mentorship**
Panelists: Drs. Nancy Baxter, Sharon Straus, Varun Kapila and Zane Cohen
1:30

Paper Session III
Chair: Dr. Mary Anne Aarts
2:30

State of the Union Address
Dr. Andrew J Smith
Bernard & Ryna Langer Chair
Division of General Surgery
University of Toronto
3:30

Paris Suite (2nd Floor)

Laparoscopic Skills Competition for CAGS Finalists
Chair: Dr. Sean Cleary
4:15

Wellesley Ballroom (Main Floor)

Cocktail Reception
4:15

Evening Program and Graduation Dinner
Master of Ceremony: Dr. Andrew Smith
Presentation of the Robert Mustard Mentorship Award
Scientific Awards: Dr. Murray F. Brennan
Graduation Ceremony: Dr. Najma Ahmed
Valedictory address: Dr. Karen Devon
Closing comments
5:30

**Concurrent Sessions**

Lunch
Paper Session

Chair:
Dr. Rebecca Gladdy

University of Toronto circa 1920

Banting & Best’s Lab
A History of Discovery
Identification of candidate familial pancreatic cancer genes by analysis of germline copy number variation

Wigdan Al-Sukhni, Sarah Joe, Ayelet Borgida, Nora Zwingerman, Aaron Gropper, Sara Moore, Heidi Rothenmund, George Zogopoulos, Steven Gallinger

Introduction/Background: Germline copy number variation (CNV) is a widespread form of genomic variation which has been linked to disease phenotypes. We proposed to identify candidate genes in Familial Pancreatic Cancer (FPC) by analyzing germline CNVs specific to high-risk pancreatic cancer patients.

Methods: Lymphocyte DNA from 124 FPC cases and 1198 controls were analyzed for CNVs using a high-resolution microarray, and findings were validated using a different SNP/CNV microarray and quantitative PCR. Regions deleted or duplicated only in cancer patients were investigated further.

Results: A stringent algorithm identified 390 CNVs in cases and 3128 CNVs in controls, with a validation rate of ≥ 90%. No significant difference was observed in CNV characteristics between cases and controls. Sixty-nine CNVs were found exclusively in cases. Fifty-five genes were partially or completely encompassed by 34 FPC-specific CNVs; 55% of genes are potentially involved in tumorigenesis, and 22% are reported to be differentially expressed in pancreatic cancer. To date, one duplication transecting an interesting gene was investigated in depth, but does not appear to segregate with the disease state in affected relatives.

Conclusions: Our CNV analysis algorithm validates well and has detected several FPC gene candidates. Investigation of potentially pathogenic CNVs in FPC is ongoing.
A novel role for the cell cycle regulator Polo-like Kinase 4 (Plk4) in cell migration and invasion

Francis SW. Zih, Carla O. Rosario, Alexandra George, Yosr Haffani, James W. Dennis, Carol J. Swallow

Introduction: In patients with colorectal cancer (CRC), Plk4 expression is increased modestly in primary tumours, and markedly in liver metastases. We recently found that haploid levels of Plk4 are associated with defective cytokinesis, related to lack of appropriate actin filament rearrangement resulting from failure to activate RhoA in mitotic cells (Rosario, PNAS, 2010). We hypothesize that Plk4 increases cellular motility via RhoGTPase activation, enhancing migration and invasion, and thereby metastatic capacity.

Methods: Plk4+/+ and Plk4+- murine embryonic fibroblasts (MEFs) were compared in expression array (Illumina), spreading, scratch wound, transwell migration and RhoA activation assays.

Results: Differences in expression pattern predicted reduced motility in Plk4+- vs. Plk4+/+ MEFs. This was validated in functional assays: Plk4+- MEFs showed impaired spreading with fewer cell protrusions (p=0.003), reduced wound healing in a scratch wound assay (p=0.025), defective directional migration (p=0.004), and impaired activation of RhoA. DLD-1 CRC cells transfected with Flag-Plk4 had a higher migration rate than Flag alone control.

Conclusions: Plk4, previously recognized as a cell cycle regulator required for centriolar duplication, also facilitates cell migration and invasion. Regulation of RhoA activation and actin rearrangement may be the underlying mechanism. Increased expression of Plk4 may contribute to metastatic potential in cancer cells.
**Regulation of cytokine signal transduction by the anti-proliferative and immunosuppressive agent Rapamycin**

Emily Partridge, James W Dennis, Vivek Rao

**Introduction:** Transplant vasculopathy (TV) is a complication of organ transplantation characterized by diffuse luminal narrowing and occlusion of the allograft vasculature, resulting in shortened graft survival. Repetitive endothelial injury by immunosuppressive drugs such as corticosteroids and calcineurin inhibitors has been implicated in the pathogenesis of TV. Rapamycin is an anti-proliferative immunosuppressive agent which has been shown to reduce TV, though the mechanism by which this occurs is poorly understood.

TGF-β1 is a cytokine known to suppress immune function and inhibit proliferation, while the RTKs are a family of cytokines which stimulate proliferation, metabolism and endocytosis. We hypothesized that rapamycin mediates its anti-TV effects through the regulation of vascular cell cytokine signaling and proliferative responses.

**Methods/Results:** We have employed quantitative immunofluorescence and Western blotting to assay phosphorylation cascades mediating intracellular cytokine signaling, and proliferation assays to quantify cell growth. Here we demonstrate that rapamycin enhances the amplitude and duration of TGF-β1 signal transduction and inhibits RTK responses in human vascular endothelial cells, with resultant inhibition of proliferation. Treatment of cells with pharmacologic inhibitors of endocytosis rescued the effects of rapamycin on cytokine signaling.

**Conclusions:** This study demonstrates that rapamycin modulates signal transduction in endothelial cells by regulating receptor endocytosis, and suggests that the clinical benefits associated with rapamycin are brought about by regulating mitogenic and proliferative cues. Further study of these signaling pathways may identify other therapeutic targets to facilitate improvements in transplant allograft survival.
Poster Session

Hosted by:
Dr. Nancy Baxter

Please refer to “Poster Presentations” section for all poster listings.
Paper Session

Chair:
Dr. Teodor Grantcharov

University of Toronto, circa 1953
Ex-Vivo Technical Skills Training Transfers to the Operating Room and Enhances Cognitive Learning: A Randomized Controlled Trial

Vanessa N. Palter, Teodor P. Grantcharov, Adrian Harvey, Helen M. MacRae

**Introduction:** Surgical training includes acquiring technical skills and cognitive knowledge. Technical skills training on simulated models has been shown to improve technical performance in the operating room (OR), and may enhance the acquisition of other skills by freeing cognitive capacity. This has yet to be investigated.

**Methods:** A single-blinded randomized controlled trial was conducted to assess the effect of ex-vivo technical skills training on cognitive learning in the OR. 18 surgical residents were randomized to two groups. Residents in the intervention group practiced fascial closure on a low fidelity model until technical proficiency was reached. All residents then performed a fascial closure on a patient in the OR while listening to a script that contained relevant clinical information. A validated evaluation tool was used to assess the technical merit of the closure. All participants completed a multiple-choice test deigned to assess the information retained from the script.

**Results:** The ex-vivo trained group performed significantly better on the cognitive retention test and showed superior technical skills compared to the un-trained group (p=0.03, p=0.04).

**Conclusions:** Technical skills training using a low fidelity simulator resulted in improved technical performance in the OR, and enhanced the ability of residents to attend to cognitive components of surgical expertise.
Introduction/Objectives: Synoptic reports improve the completeness of pathology reporting, but it remains unknown whether they eliminate reporting discrepancies between gastrointestinal and non-gastrointestinal pathologists.

Methods: A total of 441 pathology reports from rectal cancer resections performed between 1997 and 2006 were identified and assessed for completeness according to a set of prognostic features. Narrative reports and those using a standardized synoptic format, which was introduced in 2001, were compared.

Results: Synoptic reports (n=226) were more complete than narrative reports (n=215) for TNM stage (92.5% v. 20.5%, p<0.001), distance to radial margin (97.6% v. 86.4%, p<0.001), tumour grade (96.9% v. 91.2%, p=0.015), lymphovascular invasion (LVI) (96.9% v. 33.0%, p<0.001), extramural venous invasion (EMVI) (95.1% v. 34.4%, p<0.001) and perineural invasion (97.7 v. 11.6, p<0.001). Narrative reports from non-gastrointestinal pathologists were less complete for LVI (50.0% v. 30.1%, p=0.027) and EMVI (59.4% v. 30.1%, p=0.001), but there was no difference in completeness once synoptic reporting was adopted. Gastrointestinal pathologists identified EMVI more frequently in both the narrative (15.6% v. 4.4%, p=0.029) and synoptic (27.4% v. 14.8%, p=0.021) formats.

Conclusions: Completeness of reporting was dramatically improved by the use of synoptic reports. However, non-gastrointestinal pathologists still identified EMVI less frequently, potentially limiting the uptake of adjuvant chemotherapy.
Clinical and pathological predictors of recurrence and outcomes of treatment following liver transplantation for hepatocellular carcinoma

Charbel Sandroussi, Markus Guba1, Lakhbir Sandhu, Derek Dubay, Anand Ghanekar, Mark S.Cattral, Ian D. McGilvray, Eberhard Renner, Markus Selzner, Paul D.Greig, David R.Grant

Introduction: There is limited data available on the biology of recurrent HCC after liver transplantation (OLT) and no recommendations for follow up. The aims of this study are to determine recurrence rates following OLT for advanced HCC, identify predictors of recurrence so that high and low risk groups can be defined and to identify patterns of recurrence and outcomes following aggressive surgical and medical treatment.

Methods: 348 consecutive patients transplanted for HCC between 1996 and 2008 were analyzed. Patients were imaged every 3-6 months for 5 years. Clinical and pathological predictors of recurrence were identified. Using these a recurrence risk score was developed. Recurrences were aggressively treated with multimodal therapy. Outcomes and predictive factors following treatment of recurrence were identified.

Results: 143/348(41.4%) of patients had tumors exceeding the Milan Criteria. The median follow up was 34.5 months. 143/348(41.1%) patients were outside the Milan Criteria. Patients were imaged every 6 months for 5 years. 5yr overall and disease free survival was 75% and 71% respectively with no significant difference for within or outside Milan tumors. Recurrence occurred in 49(14.1%) patients (Milan 7.6% vs outside 22.5%; p=0.001), 73.5% were within 2 years. 69.4% had a single site of recurrence. The commonest sites of recurrence were locoregional (49%) and chest (49%). Median survival after recurrence was 8.7 months (0-81) and 1, 3 and 5 yr survival was 47%, 14% and 14% respectively, increasing to 38% if recurrence was resectable. On univariate logistic regression analysis α-FP>400 (p=0.008), progression with treatment (p=0.004), number (p=0.001) size and total tumor diameter (p<0.001), macro and micro vascular invasion (p<0.001), beyond Milan (p<0.001) and a >50% increase in α-FP (p<0.001) were predictive of recurrence. The recurrence score accurately predicted recurrence (p=0.001) and disease free survival after OLT (p=0.01). On multivariate analysis Milan post transplant (OR 0.294; p=0.042) and a >50% increase in α-FP (OR 59.545; p=0.001) remained predictive of recurrence. On uni and multivariate Cox regression only time to recurrence (HR 0.978; p=0.018) and surgical treatment (HR 0.243; p=0.006) were associated with improved survival.

Conclusions: It is possible to achieve long term survival following recurrence of HCC after OLT with an aggressive multimodal therapy which includes surgery. Most recurrences occur within 3 years and this study provides rationale for surveillance in high risk patients with both cross sectional imaging and α-FP every 6 months for 5 years and then α-FP alone thereafter.
Objective: To assess practice patterns among general surgeons (GS) and medical oncologists (MO) who refer patients with hepatic colorectal cancer (CRC) metastases to HPB surgeons.

Methods: A postal survey was sent to GS (n=628) and MO (n=147) in Ontario. The questionnaire examined approaches to referral and perceived contraindications to hepatectomy for CRC metastases.

Results: The overall response rate was 52% (GS 51%; MO 56%). 74% of physicians “very often” or “always” refer patients with hepatic CRC metastases to HPB surgeons but 24% “rarely” or “sometimes” do so (GS 23%, MO 25%). 97% of physicians reported referring patients with single liver lesions “very often” or “always.” Only 28% would refer patients with bilateral, multiple CRC metastases (GS 29%, MO 25%). Whereas only 2% of MO (n=1) “never” refer patients with bilateral, multiple lesions for surgical consideration, 17% of GS (n=36) never do so (p=0.01). Perceived contraindications to surgery were similar across both groups: 25% of physicians consider a previous liver resection a contra-indication to hepatectomy, as compared to 41% for lung metastases, and 63% for extra-hepatic metastases.

Conclusions: While patients with single CRC liver metastases are receiving appropriate HPB surgical consultations, the rate of referral declines as the burden of disease increases.
Poster Session

Hosted by:
Dr. Avery Nathens

Please refer to “Poster Presentations” section for all poster listings.
The E. Bruce Tovee Lecture
“Lessons Learned from Mentor to Deuteronomy”

Born in Auckland, New Zealand, Dr. Murray Brennan received a degree in mathematics from the University of New Zealand and a medical degree from the University of Otago in 1964. In 1970 he worked with Francis D. Moore, MD at Peter Bent Brigham Hospital, Harvard Medical School and with George F. Cahill Jr., MD at the Joslin Research Laboratories. After residency at the Brigham, Dr. Brennan joined Steven Rosenberg, MD at the National Cancer Institutes where he was Head of the Surgical Metabolism Section. In 1981, he joined Memorial Sloan-Kettering Cancer Center (MSKCC) as Chief of Gastric and Mixed Tumor Service. Dr. Brennan was Chairman of the Department of Surgery at Memorial Sloan Kettering Cancer Center from 1985 until June 2006. He currently holds the Benno C. Schmidt Chair in Clinical Oncology and was recently appointed Director of the International Center and Vice President for International Programs at MSKCC.

In 1995, Dr. Brennan was honored with membership in the Institute of Medicine of the National Academy of Sciences and in 2000 with the American College of Surgeons’ highest award, The Distinguished Service Award. He holds Honorary Doctorates from the University of Edinburgh, Imperial College London, University of Goteborg, and the University of Otago in New Zealand. He also has received Honorary Fellowships from the Royal College of Surgeons of Edinburgh, Glasgow, Canada, England, Australia, Ireland and others. He has lectured throughout the world and authored and co-authored more than 1,000 scientific papers and book chapters focusing on surgical oncology, endocrinology, metabolism, and nutrition, and is the author of a book on soft tissue sarcoma.

Dr. Brennan’s interest in addition to patient care and research has been the development of young surgeons. His ‘fellows’ now hold leadership positions throughout the world.

2010
E. Bruce Tovee Invited Lecturer
Murray F. Brennan, MD, FACS.
Paper Session

Chair:
Dr. Mary Anne Aarts
Introduction/Objective: Injured patients cared for in trauma centers (TC) have lower mortality than those cared for in non-trauma centers (NTC). However, half of TC patients are first cared for at NTC (undertriaged). Previous analyses of undertriage have been subject to survivor bias. Unbiased assessments of the mortality attributable to undertriage might influence system policy.

Methods: We performed a retrospective cohort study of severely injured patients presenting to hospital in Ontario. Undertriaged patients were those triaged to a NTC. Undertriaged patients were either transferred to a TC (transfer) or died before transfer could be accomplished (ED-death). The remaining patients were transported directly (direct) to a TC. 30-day mortality among undertriaged patients was analyzed using two approaches: allowing for survivor bias (comparing transfer vs. direct) and without survivor bias (undertriaged vs. direct).

Results: Among 11,398 patients, only 66% were transported directly to a TC. Ignoring survivor bias, mortality in the transfer and direct groups was equivalent. Unbiased assessment demonstrated mortality was significantly higher in the undertriaged cohort than the direct cohort (OR 1.24, 95% CI 1.10-1.40).

Conclusions: Undertriage following major trauma is associated with significantly higher mortality than previously thought. These data suggest a need to design strategies to improve triage to TC.
Two founder MSH6 mutations associated with inherited cancer susceptibility in Ashkenazi Jewish population

Frank Schwenter, Leon Raskin, Marina Freytsis, Faina Bogomolniy, Melyssa Aronson, Gad Rennert, Steven Gallinger, Douglas A. Levine, Marc Tischkowitz, Stephen B. Gruber, William Foulkes

Introduction/Objective: Mutations in DNA mismatch-repair genes are the cause of cancers associated with Lynch syndrome. The most common mutations affect MLH1 and MSH2 genes, while the MSH6 gene is less commonly involved. We report here two MSH6 founder mutations in the Ashkenazi Jewish (AJ) population.

Methods: MSH6 exon 9 insertion and deletion mutations were analyzed in cancer patients and healthy controls of AJ descent in Canada, USA and Israel. The frequency of the mutations and the range of malignancies were evaluated. Microsatellite markers and single nucleotide polymorphisms were analyzed in carriers.

Results: Among 2660 population-based AJ colorectal cancer cases (CRC), 8 carried a 4 bp duplication mutation (0.3%), and 3 carried a 4 bp deletion mutation (0.1%) in exon 9 of the MSH6 gene. In comparison, 1 duplication (0.03%) and no deletion were observed in 3270 control individuals. In a hospital-based series of 79 CRC, one individual carried the deletion, but no duplication were seen. Among 136 endometrial cancer cases, 2 carried the duplication. In a series of pancreas cancer cases, 1 individual carried the deletion. Haplotype analysis confirmed founder mutations.

Conclusions: These rare founder MSH6 truncating mutations are of great importance for the screening, genetic counseling and follow-up of AJ families presenting malignant tumors compatible with Lynch syndrome.
Regional variations in access to definitive trauma centre care

David Gomez, Barbara Haas, Brandon Zagorski, Joel Ray, Gordon Rubenfeld, Avery B. Nathens.

Introduction: Inclusive trauma systems ensure that injured patients are transported to the right place at the right time through the use of triage and inter-facility transfer criteria. However, a significant proportion of severely injured patients who receive initial care at non-trauma centers (NTC) never receive definitive trauma center (TC) care. The aim of this study was to identify and characterize regional patterns of access to TC care.

Methods: We used a series of population-based datasets to identify severely injured patients. Lack of access to TC care was defined as admission or death in the ED of NTCs. Data were aggregated at the county level and a geographic information system was used to explicate regional TC access patterns.

Results: We identified 19,541 severely injured patients, 42% of patients never had access to TC care (n=8,227). There was significant variability in the proportion of patients without access to TC across counties, ranging from 0% to 91% (median 54%, IQR 33-65%). In regions with a TC, 12% of patients had no access to that center (range 0-35% across counties with a TC).

Conclusions: After an injury, patients should be preferentially transported to institutions that specialize in caring for injured patients (i.e. trauma centres). However, a significant proportion of injured patients never have access to definitive trauma centre care. We used a series of population-based datasets in order to characterize regional patterns of access to trauma centres. We identified that 42% of injured patients never access trauma centres; however, there was significant regional variation in lack of access.
Introduction: Current Canadian breast screening guidelines recommend mammogram and clinical breast exam every two years beginning at age fifty. This study evaluates the contribution of clinical examination by experienced practitioners to screen detected cancer rates.

Methods: 5000 clinical breast examinations of asymptomatic women were reviewed. Each was prospectively recorded using standardized notation. Age, menstrual and childbearing history, family history of breast or ovarian cancer, use of hormonal therapy, and menopausal status were all recorded. Women with prior breast cancer were excluded. All women underwent clinical exam and 2 view mammography.

Results: 458 mammogram detected abnormalities required follow-up and led to a diagnosis of cancer in 12%. Clinical breast exam was abnormal in 98 of 5000 cases and correlated with invasive cancer on final diagnosis in 13%. Each invasive cancer detected by clinical breast exam was also detected by mammogram. Clinical breast exam did not identify additional malignancy, and resulted in 61 callbacks in women with normal imaging.

Conclusions: In an asymptomatic screening population, clinical breast exam by experienced practitioners had no additional benefit over mammography in cancer detection, and led to unnecessary follow up investigations.
1. Oncologic outcome in ulcerative colitis patients with dysplasia or cancer who underwent stapled or hand-sewn ileal pouch anal anastomosis. Wigdan Al-Sukhni, Robin McLeod, Helen MacRae, Brenda O’Connor, Harden Huang, Zane Cohen.


3. Polo-like kinase 4 (Plk4) enhances expression of the matrix degrading metalloproteinases MMP-13, -10 and -3 and promotes invasion through basement membrane. Olga Brashavitskaya, Carla Rosario, Yosr Haffani and Carol J. Swallow.


7. A 3D computer animation to enhance surgical resident understanding of the axillary lymph node dissection (ALND) procedure. Fung, A, McCready, DR Cil, T.

8. Predictors of peri-operative morbidity and liver dysfunction after liver resection in patients with chronic liver disease. Elisa Greco, Sulaiman Nanji, Alice Wei, Paul Greig, Steven Gallinger, Sean Cleary.


11. Value of laparoscopy in children with a suspected rotation abnormality on imaging. Marvin Hsiao, Alan Daneman, Jacob C. Langer


16. Towards an Understanding of the Psychosocial Reactions to Surgeon Error: A Literature Review. Shelly Luu, Jenny Jin, Annie Leung, Maria Athina Martiminakis, Catherine Merritt, Steven Gallinger, Carol-anne Moulton


20. Sociodemographics and comorbidities influence decisions to undergo pancreatic resection for neoplastic lesions. Charbel Sandroussi, Chantelle Brace, Erin Kennedy, Nancy Baxter, Steve Gallinger, Alice Wei


22. Non technical skills assessment in the post operative setting. Sharma B, Orzech N, Grantcharov T.


26. A cost-minimization analysis (CMA) of sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND) in Ontario. Wells BJ, Quan ML, Coyte P.


30. The Efficacy of Diet and Exercise on Improving Quality of Life for Colorectal Cancer Survivors: A Systematic Review of the Literature. Nafisha Lalani, Erin Kennedy, Carol Swallow
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The Annual Assembly of General Surgeons

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