Hawai‘i Chapter
Scientific Meeting 2019

The Art of Being an Internist

Saturday, February 23, 2019
Pomaika'i Ballrooms at Dole Cannery
Honolulu, HI

This live activity has been designated for 6.25 CME credits and 6.25 MOC points.
Learning Objectives
At the conclusion of this activity, the participant will be able to:
- Apply updated knowledge of Internal Medicine to clinical practice.
- Apply updated knowledge of Cardiology, Critical Care, Hematology/Oncology, and Infectious Diseases to clinical practice.
- Improve clinical practice by incorporating major new developments in Cardiology, Critical Care, Hematology/Oncology and Infectious Diseases.
- Understand recent advances in Internal Medicine.
- Understand recent advances in Cardiology, Critical Care, Hematology/Oncology and Infectious Diseases.
- Improve diagnosis and management in Infectious Diseases.
- Increase confidence in performing clinical skills.
- Increase confidence in performing in Bedside Clinical Exam.
- Increase confidence in medical computing.
- Understand political advocacy and reform.

CME Accreditation and MOC Points
The American College of Physicians is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The American College of Physicians designates this live activity for a maximum of 6.25 AMA PRA Category 1 Credit(s)™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.
Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 6.25 medical knowledge MOC points in the American Board of Internal Medicine’s (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credit claimed for the activity. It is the CME activity provider’s responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Your Opinion Counts
At the conclusion of the meeting, please take a moment to complete the meeting survey form and verification of attendance form in your packet and return it to the registration desk. We value your opinion and use the surveys in planning future meetings.

Chapter Excellence Award
We are pleased to announce that our chapter is in receipt of the 2018 Chapter Excellence Award. The Chapter Excellence Award recognizes those chapters that excel in reaching the standards for managing a chapter, such as communicating to members, instituting Medical Students’ and Resident/Fellow Members’ activities and advancing and recruiting members.

Resident/Fellows’ and Medical Students’ Activities
Clinical vignettes, posters, and research papers prepared by Resident/Fellow Members and Medical Students will be presented at the meeting. Winners will receive a cash prize and be eligible for entrance into the national competition held during the ACP Internal Medicine National Meeting 2019.
Pathways to Fellowships

Attendance at chapter meetings can help all ACP members meet the qualifications for advancement to Fellowship. It is especially important for those applying under the pathway that calls for five years of activity as a member.

Governor

Lisa A. Camara, MD, FACP
ACP Governor, Hawai’i Chapter
Email: Lisa.A.Camara@kp.org

Program Committee

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David Hostler, MD, FACP, Tripler Army Medical Center, Honolulu

John Houk, MD, FACP, Assistant Clinical Professor, Department of Medicine, University of Hawai‘i, Honolulu

Laura Houk, MD, Intern University of Hawai‘i Residency Program, Honolulu

William Loui, MD, FACP, Assistant Clinical Professor, Department of Medicine, University of Hawai‘i, Honolulu

Between scientific sessions please visit the College table where you can find information on new ACP programs, and many other products. There’s always something new at the College table. Stop by and see for yourself.
LAUREATE AWARD WINNER:
Dr. John Houk, MD, FACP

Dr. John Houk was born and raised in Chicago, Illinois, where he graduated cum laude from Beloit College. He attended medical school at the Abraham Lincoln School of Medicine at the University of Illinois, and completed his Internal Medicine residency at Parkland Memorial Hospital at the University of Texas, Southwestern, in Dallas, Texas.

Thus began the medical career of what the Honolulu community came to recognize as a singularly dedicated and visionary physician.

After relocating to Hawai‘i in the 1980s, Dr. Houk promptly became teaching faculty at UHIMRP while maintaining a busy practice at the Fronk Clinic. Within a span of 2-3 years, Dr. Houk became Chair of the Department of Internal Medicine and Chair of both the Recruitment and By-Laws committees.

After the dissolution of Fronk Clinic, Dr. Houk began his successful private practice at the Queen’s Medical Center, all the while maintaining his active participation in the American Medical Association (AMA), Hawai‘i Medical Association (HMA), Honolulu County Medical Society (HCMS), American Society of Internal Medicine (ASIM), Hawai‘i Society of Internal Medicine (HSIM), and of course, the American College of Physicians (ACP). He had leadership positions in several of these professional societies – a full list would be time and space prohibitive – but notable mentions would be the president of HSIM (1989-91), and HMA’s Physician of the Year (2012).

He’s been medical director of Arcadia and 15 Craigside, continuing care retirement communities, since 1990, and in his “spare time”, founded Primary Care Physicians of Hawai‘i and Hawai‘i Independent Practice Association.

Dr. Houk has consistently demonstrated a keen vision for developments in the field of medicine, and early on was a proponent of establishing a Medical Home and in more recent years, a plant-based diet as a healthy lifestyle choice. He has always been a clinician-educator, and has mentored countless medical students and residents over the years.

The Laureate Award honors Fellows or Masters of the ACP who have demonstrated, by their example and conduct, an abiding commitment to excellence in medical care, education, and service to their community, their Chapter, and to the ACP. It is because of his distinguished career and dedication to his patients and community, and to educating students and residents, that Dr. John Houk has been chosen as the 2019 Laureate for the Hawai‘i Chapter.
Program - Saturday, February 23, 2019

7:30 a.m.
Check-in/Poster Judging

7:50 a.m.
Governor’s Welcome
Lisa A. Camara, MD, FACP

Program Chair
Kuo-Chiang Lian, MD

8:00 a.m.
Podium Presentations (2)
Moderator: Elizabeth K. Tam, MD, FACP

8:00 a.m. Young Soo Rho M.D.
Associated Factors and Survival Implications of Biopsy Diagnosis of Hepatocellular Carcinoma

8:15 a.m. Andrew Ko, BS
Cell-To-Cell Propagation of Cell Death Induced by Excess Iron in Cardiomyocytes

8:30 a.m.
Session #1 – Catheter Ablation for Atrial Fibrillation?
Robert Hong, MD
Osamu Fukuyama, MD, FACP

9:30 a.m.
Break/Poster Judging
Break – Resident/Medical Student Social Breakout

10:00 a.m.
Session #2 – “5 Easy Steps to Improve Critical Thinking”
William Loui, MD, FACP

11:00 a.m.
Podium Presentation (2)
Moderator: James Epure, MD, FACP

11:00 a.m. Wakako Horiuchi
Health Care-Seeking Behaviors of Medicare Beneficiaries with Functional Hearing Loss

11:15 a.m. Selin Kutlu
The Relationship Between Comorbidities and Enrollment in Cancer Clinical Trials by Age at Diagnosis

11:30 a.m.
Dr. Irwin J. Schatz, MD, MACP Lectureship – VBC - Value Based Care or Very Burnt-Out Clinician?
John Houk, MD, FACP
Laura Houk, MD
Business Meeting/Lunch/Posters

1:00 p.m.
Podium Presentation (2)
Moderator: Jim Ireland, MD, FACP

1:00 p.m. Elisabeth Seamon, MPH
Cerebral Aging-Related TDP-43 with Sclerosis (CARTS) – Diagnostic or Random?

1:15 p.m. Roxanne Ko, BA, BS
Prevalence of Substance Use and Substance Use Disorder Among Middle-Aged and Older Adults with Multiple Chronic Conditions in the United States

1:30 p.m.
Session #3 – Volume Assessment? Wet or Dry?
Benjamin W. Berg, MD FACP
David Hostler, MD, FACP

2:30 p.m.
Break/Poster Judging
Physician Networking

3:00 p.m.
Podium Presentations (2)
Moderator: Don Helman, MD, FACP

3:00 p.m. Andrew Pham, BS
Distinction Between Mitophagy and Ferroptosis in Cardiomyocytes

3:15 p.m. Robert J. Pattison, MD, MPH
Characterization of Chronic Liver Disease in Hawai‘i Using Transient Elastography

3:30 p.m.
Session #4 – Infectious Disease: Tips for Bedside Diagnosis
Joel D. Brown, MD, FACP

4:30 p.m.
Awards
Medical Jeopardy
Pau Hāna
PODIUM PRESENTATIONS
ASSOCIATED FACTORS AND SURVIVAL IMPLICATIONS OF BIOPSY DIAGNOSIS OF HEPATOCELLULAR CARCINOMA

Young Soo Rho M.D., Jared Acoba M.D.
University of Hawai‘i, Internal Medicine Residency Program

Background: Hepatocellular carcinoma (HCC) is one of the few cancers that can be diagnosed based on image findings alone. However, biopsy of HCC can confirm histologic subtype, and potentially be used to identify novel therapies. The factors associated with undergoing a biopsy diagnosis and the difference in survival between patients diagnosed with imaging versus biopsy have never been studied.

Methods: We collected demographic, diagnostic, treatment, and survival data of 171,013 patients diagnosed with HCC between 2004 – 2015 from the National Cancer Database. To determine factors associated with undergoing a biopsy, binary logistic regression was performed. Univariate and multivariate cox proportional hazards regression models were created to determine impact of diagnostic method on survival. Variables included were race, sex, age, comorbidity, facility type (academic vs community), insurance, tumor size, presence of metastatic disease, alpha fetoprotein, total bilirubin, and administration of therapy. Analysis was performed with SPSS v25.

Results: We included 160,517 patients in the final analysis. The median age was 62 (18–90), 73.9% were male and 74.1% were white. 11.5% of tumors were 2cm or smaller and 13.7% of HCC were metastatic. 78,485 (47.7%) underwent a biopsy. In a multivariate model, black patients (OR 1.093; 95% CI 1.061–1.126), older patients(OR 1.579; 95% CI 1.537–1.622), larger tumor size (OR 3.208; 95% CI 3.085 – 3.335), private (OR 1.129; 95% CI 1.094–1.164) or Medicare insurance(OR 1.056; 95% CI 1.021 – 1.093), and metastasis (OR 1.318; 95% CI 1.275–1.361) were associated with biopsy diagnosis. Factors associated with an imaging diagnosis were female (OR 0.964; 95% CI 0.941–0.987), Asian/Pacific Islanders (OR 0.686; 95% CI 0.657–0.717), higher comorbidity index (OR 0.578; 95% CI 0.559–0.597), treatment at an academic center (OR 0.447; 95% CI 0.436 – 0.458), hyperbilirubinemia (OR 0.807; 95% CI 0.784-0.831) and elevated AFP (OR 0.571; 95% CI 0.549-0.594). Over the examined study period 2004–2015, imaging diagnosis was increasingly used. Patients who underwent biopsy demonstrated inferior survival with a HR 1.400 (95% CI: 1.385–1.417). After adjusting for other prognostic factors in a multivariate cox analysis model, biopsy had a much smaller impact on survival HR 1.017 (95% CI: 1.004–1.030).

Conclusions: Although imaging alone can be adequate to diagnose many cases of HCC, nearly half of the cohort underwent a biopsy. While the diagnosis by imaging was more frequently used in recent years, there were still racial and institutional differences in pattern of care. Establishing a diagnosis with a biopsy did not have a significant impact on survival.
CELL-TO-CELL PROPAGATION OF CELL DEATH INDUCED BY EXCESS IRON IN CARDIOMYOCYTES

Andrew Ko, BS, Nicholas Kawasaki, BS, Motoi Kobayashi MD, PhD, and Takashi Matsui, MD, PhD;
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Advances in treatment of myocardial infarction (MI) have greatly reduced mortality from acute events. However, heart failure (HF) following MI remains a major contributor to morbidity and mortality. Adverse remodeling, a key pathophysiological feature of HF, is directly correlated with the magnitude of cardiomyocyte (CM) cell death caused by acute MI. We and other groups reported a positive correlation between iron deposition and adverse remodeling in ischemia-reperfusion (I/R) injury. Our previous studies also showed that cell-to-cell death along myofibers is consistently observed in I/R injury models.

Mitochondrial reactive oxygen species (ROS) is known as a major factor for cell death induced by excess iron. Ferroptosis, an iron-dependent form of regulated cell death, is induced by suppressing glutathione peroxidase 4 (GPX4), an enzyme that inhibits accumulation of lipid ROS. At the previous ACP meeting, we reported that RSL-3, a GPX4 inhibitor, demonstrated “clusters” of death in CMs consistent with the cell-to-cell death hypothesis. However, cell-to-cell death in in vitro CMs exposed to excess iron is not well-characterized. To further investigate the role of iron-mediated cell death in CMs, we assessed the pattern of cell death caused by iron (III) citrate in a dose-dependent manner. Cell death patterns caused by iron was compared to that induced by hydrogen peroxide (H2O2), a ROS species produced in mitochondria that is broadly used as a trigger of CM cell death in I/R injury studies.

We cultured H9c2 cells, derived from embryonic rat ventricles, in 12-well plates containing DMEM with 10% FBS to 90% confluency in 5 mM, 10 mM, 20 mM, and 30 mM iron (III) citrate. Controls were set up without iron (III) citrate and treated with either 50 ng/mL RSL-3 or 20 uM H2O2. Cell death was analyzed with Live/Dead Cell Viability Assay and randomized images were taken under fluorescent microscopy. Experiments showed that cells cultured in increasing concentrations of iron (III) citrate tended to demonstrate a diffuse pattern of cell death, similar to cells treated with H2O2; in contrast, cells cultured in lower concentrations of iron (III) citrate tended to demonstrate a more clustered pattern of cell death, similar to cells treated with RSL-3.

This study suggests that specific concentrations of iron can effectively induce in vitro cell-to-cell death as seen in ferroptosis. Further investigation using this model may elucidate a therapeutic target aimed at stopping damage from extending past the initial area of infarction during an MI. Minimizing this area of injury will reduce morbidity and mortality from subsequent HF.
HEALTH CARE-SEEKING BEHAVIORS OF MEDICARE BENEFICIARIES WITH FUNCTIONAL HEARING LOSS

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Background: Hearing loss has implications on poor health outcomes. This study explores the consequences of functional hearing loss on health access through the health care-seeking behaviors of older adults.

Methods: This is a cross-sectional cohort study of a nationally-representative sample of community-dwelling Medicare beneficiaries using the 2015 Medicare Current Beneficiary Survey. Functional hearing loss was identified from self-reported trouble hearing. Multivariate logistic regression analyzed outcomes including perceived delay in accessing care, seeking immediate care, disclosing illness to others, worrying about health, avoiding treatment, and attempting to seek care for the delayed problem.

Results: Of the 10,848 participants included in the study, 4,429 (40.8%) had a little trouble hearing and 801 (7.4%) had a lot of trouble hearing. Controlling for predisposing characteristics, enabling factors, and perceived need for care, participants with a little (OR=1.61; 95% CI=1.33-1.95, p<0.0001) or a lot of trouble hearing (OR=2.01; 95% CI=1.44-2.80, p<0.0001) were found to have significantly greater odds of delaying health care. Conversely, those who reported hearing aid use had significantly decreased odds (OR=0.55; 95% CI=0.39-0.78; p<0.001) of delaying health care as compared to those with no trouble hearing. Participants with a little trouble hearing had decreased odds of seeking medical attention immediately upon feeling sick (OR=0.77; 95% CI=0.68-0.88; p<0.0001) and increased odds of keeping information about illness to themselves (OR=1.15; 95% CI=1.01-1.33; p<0.05). No significant differences in odds were found in functional hearing loss and worrying about health, avoiding treatment, and attempting to obtain care for the delayed problem.

Conclusions: Hearing loss is independently associated with a perceived delay in accessing health care. The care-seeking behaviors of Medicare beneficiaries with hearing loss suggest that there may be systematic deterrents that contribute to the perceived delay. Hearing aids may improve these health care-seeking behaviors among Medicare beneficiaries with hearing loss.
THE RELATIONSHIP BETWEEN COMORBIDITIES AND ENROLLMENT IN CANCER CLINICAL TRIALS BY AGE AT DIAGNOSIS

Selin Kutlu¹, Dina G. Lansey, MSN, RN², Norma F. Kanarek, PhD, MPH³
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Background: Cancer clinical trial (CCT) eligibility criteria are major barriers to participation. Even though the majority of cancer patients are older than 65 years, they are underrepresented in CCTs. Since comorbidity associates with aging, we calculated the prevalence of specific comorbidities and assessed whether any limit enrollment by age groupings.

Methods: Cancer patients diagnosed at Sidney Kimmel Comprehensive Cancer Center were identified from the Johns Hopkins Hospital cancer registry. To evaluate CCT enrollment, 17,959 patients residing in the United States first seen between 2014 and 2016 were examined on age (18 to 39, 40 to 64, 65 to 84, older than 85 years), sex, race (white, black, other), residence (Baltimore City, Maryland, Maryland-adjacent states, other), cancer characteristics and specific comorbidities (heart disease/hypertension (HTN), cerebrovascular disease, respiratory disease, hepatic disease, renal disease, diabetes, HIV, prior cancer, tobacco use). Chi-square and logistic regressions evaluated relationships among age, comorbidities and CCT enrollment. Multinomial logistic regression of CCT enrollment by age (adjusted by demographics and residence) evaluated effects for each age subgroup.

Results: 79% of patients had comorbidities, most commonly tobacco use (45%) and HTN (29%). Comorbidities were most prevalent in ages 40 to 64 (49%) and 65 to 84 (41%). Patients 85 and older enrolled significantly less than those 18 to 39 (OR 0.5, p = 0.005). In multinomial modeling, only black race enhanced enrollment in the 85 and older subgroup. In the 65 to 84 subgroup, HTN, prior tobacco use, prior cancer, female sex and Baltimore City residence suppressed enrollment. In the 40 to 64 subgroup, Baltimore City residence, female sex, HTN, respiratory disease, and other comorbidities were significantly associated with enrollment.

Conclusions: Study eligibility criteria should be reexamined to assess whether patients 40 to 84 years old with HTN, respiratory disease, tobacco use or prior cancer can safely be included in CCTs. By reconsidering study criteria and patient features such as age and comorbidities, cancer centers will have more representativeness in CCT enrollees, ultimately bringing more relevance to results.

Support: This study was supported by the NIA#2T35AG026758 Medical Student Training in Aging Research (MSTAR) Summer Program, the Maryland Cigarette Restitution Fund Research Grant at Johns Hopkins, and the Cancer Center Support Grant (P30CA006973).
Background: TAR DNA binding protein-43 (TDP-43) is normally restricted to the nucleus, but can be transported into the cytoplasm via granules due to certain stimuli. A cytoplasmic TDP-43 accumulation from a dysregulation of this process has been linked to various diseases. Hippocampal Sclerosis (HS) and the recently described Limbic Associated TDP-43 Disease (LATE) are examples of such diseases resulting in an Alzheimer’s disease (AD) presentation. To date, HS or LATE are diagnoses of exclusion where demented patients do not have AD-like cerebral spinal fluid or neuroimaging changes in abeta or tau. Cykowski et al. (2017) suggested expanding TDP-43 disease into the Cerebral Aging-Related TDP-43 with Sclerosis (CARTS) diagnostic criteria: >85 years, Braak neurofibrillary tangle stage <IV, pathological TDP-43 in the hippocampus or related regions, and exclusion of frontotemporal dementia. This project studied the prevalence of CARTS among a brain bank sample to evaluate the new criteria.

Methods: 149 brain donation samples (ages 42 - 104 years) from the Alzheimer’s Disease Research Center at UCSD were selected based on the above criteria. The hippocampal samples were sliced, prepared on slides from stored paraffin-fixed tissue, and TDP-43 stained. A slide was TDP-43 positive if 1 stained inclusion was found. TDP-43 positive demographics were analyzed.

Results: Of the 149, 14 were TDP-43 and therefore CARTS positive. The average age was 90 years. The average brain weight was 1,099 grams compared to an estimated normal brain weight at 90 years of 1,495 grams and 9 had dementia. Only 8 (58.7%) had TDP-43 disease and all Braak stages were represented.

Conclusion: CARTS did not expand TDP-43 disease as intended since all Braak stages were represented. In addition, CARTS is not specific for TDP-43 disease due to the low number of diagnosed HS within the positive group. Although CARTS is unreliable, a diagnosis for demented patients not explained by AD would have research and treatment impacts. Limitations include the subjectivity of TDP-43 grading, the small unilateral section of brain sampled, patients having overlapping pathologies, and volunteer bias. Future studies include the standardization of TDP-43 reading, phospho- versus regular TDP-43 antibodies, and staining of other brain sections.
PREVALENCE OF SUBSTANCE USE AND SUBSTANCE USE DISORDER AMONG MIDDLE-AGED AND OLDER ADULTS WITH MULTIPLE CHRONIC CONDITIONS IN THE UNITED STATES

Roxanne Ko, BA, BS,1; Benjamin Han, MD, MPH,2; Joseph Palamar, MPH, PhD,2
1University of Hawai‘i, 2 New York University

Background: Older adults are particularly vulnerable to the adverse effects of illicit drugs, as they are more likely to have multiple chronic conditions (MCC) and take more prescribed medications. Substance use can also negatively affect the management of chronic diseases.

Methods: We examined cross-sectional aggregated data from 2 annual administrations (2015-2016) of the National Survey on Drug Use and Health (NSDUH) to analyze associations between self-reported past-year drug use and multiple chronic medical conditions. We considered 10 self-reported chronic conditions queried in NSDUH and categorized the number of chronic conditions (0, 1, or >2) related to each illicit drug used (past-year use and SUD) including cannabis, cocaine, methamphetamine, inhalants, hallucinogens, heroin, and prescription opioid, tranquilizer, sedative, and stimulants. Logistic multivariable regression models were used to examine correlates of MCC among past-year drug users.

Results: The study sample included 17,571 adults age ≥50. Among adults with chronic conditions, past-year drug use was reported by 10.1% with 0 chronic conditions, 9.0% with 1 chronic condition and 9.4% with ≥2 chronic conditions (p=0.20). Past-year SUD was reported by 0.9% with 0 chronic conditions, 1.0% with 1 chronic condition and 1.3% with ≥2 chronic conditions (p=0.07). Prescription sedative and stimulant misuse was significantly higher among adults with ≥2 chronic conditions compared to those with 0 or 1 conditions. Any SUD excluding cannabis was significantly higher among adults with ≥2 chronic conditions (1.1%) compared to adults with 0 (0.6%) and 1 (0.7%) conditions (p=0.03). In the adjusted model, among adults with >2 conditions, correlates of past-year drug use included younger age, male sex, and past-year nicotine dependence and alcohol use disorder (AUD).

Conclusion: In this nationally representative survey, among adults age ≥50, there were no significant differences in the prevalence of substance use and SUD between adults with 0, 1, or >2 chronic conditions, suggesting that this cohort continues substance use even while having chronic conditions. Among adults with MCC, nicotine dependence AUD, were associated with drug use. This group with high multimorbidity may be particularly vulnerable to the negative effects of illicit substances (e.g., unintentional injuries, adverse impact on chronic disease management).
DISTINCTION BETWEEN MITOPHAGY AND FERROPTOSIS IN CARDIOMYOCYTES

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Cardiovascular disease is the leading cause of death in the US, frequently involving myocardial infarction (MI). While the extent of injury rests on the duration of ischemia, reperfusion itself damages cardiomyocytes further. In myocardial ischemia reperfusion (I/R) injury, accumulation of reactive oxygen species (ROS) is a significant trigger of cell damage. Damaged mitochondria, a major source of ROS following I/R, can be specifically eliminated by mitophagy, a type of autophagy that maintains homeostasis by removing protein aggregates and damaged organelles, to protect the heart from reperfusion injury.

We previously reported significant accumulation of iron (Fe) in the border zones of myocardial scarring in Post-MI hearts. Fe overload increases ROS production through the Fenton reaction in mitochondria. A new form of Fe-dependent cell death, ferroptosis, relies on the accumulation of lipid ROS (L-ROS) derived from Fe metabolism. Although a previous study reported that ferroptosis is a key pathophysiological factor in I/R injury, the mechanisms of ferroptosis in cardiomyocytes are not characterized well.

Both mitophagy and ferroptosis are similar in that they both involve cell death relating to excess ROS. Understanding the differences between the two pathways can help narrow targets for therapeutic treatments of I/R injury. To confirm the relationship between mitophagy and ferroptosis, we evaluated activation of mitophagy using mito-Keima, a mitophagy indicator, in multiple pathological settings: (1) starvation for autophagy, (2) Ras Selective Lethal 3 (RSL3), a ferroptosis inducer, for ferroptosis and (3) excess iron for activation of both mitochondrial and lipid ROS.

H9c2 cells, derived from embryonic rat ventricles, were transfected with 10 µL of adenovirus containing mito-Keima for 24 hours. Cell death was induced by either starvation, incubation with 10 mM Fe(III) citrate for 24 hours, or incubation with 100 ng/mL RSL3 for 5 hours. Cells were imaged under a fluorescent microscope to detect changes in the mito-Keima protein, which would infer the presence of mitophagy. Compared to the starvation conditions, cells incubated under the Fe(III) citrate and RSL3 conditions contained very low levels of fluorescence as seen in the cells with no treatment.

The results indicate no mitophagy occurrence in wells expected to undergo ferroptosis. This suggests that the process of mitophagy is distinct from ferroptosis. Further studies would be to assess the efficacy of targeting Fe, such as Fe chelators, in I/R injury. Therapeutic interventions involving control of excess ROS from I/R in mitophagy or ferroptosis may reduce morbidity and mortality in MI patients.
Introduction: Nonalcoholic fatty liver disease (NAFLD) is rapidly becoming the leading indication for liver transplantation in the U.S. Amongst those with non-cirrhotic Chronic Liver Disease (CLD), NAFLD has been found to be the most common cause of CLD in Japanese Americans, and Native Hawaiians, followed by Latinos and Caucasians. Prevalence rates of NAFLD are speculated to be even higher in “westernized Asian populations” making this even more concerning for the population in Hawai‘i. Risk stratification of patients with NAFLD is essential in preventing progression. Transient elastography using FibroScan® is particularly useful in stratifying patients with CLD as it is noninvasive and gives real-time results in regard to hepatic fibrosis and level of fatty changes. While hepatitis B (HBV) and hepatitis C (HCV) are readily diagnosed and well established as major causes of cirrhosis, NAFLD represents an insidious disease without a clear path forward for the primary care provider (PCP) or the patient.

Aim: We hypothesized that a bias against NAFLD would be reflected in referrals for Fibroscan® testing.

Methods: This study was approved by the Queen’s Medical Center Institutional Review Board as a retrospective study looking at Fibroscan® results of approximately 1101 patients between July 2013 and November 2018 conducted at Queen’s Liver Center. Patients were de-identified, grouped by diagnosis, age, gender, Controlled attenuation parameter (CAP) score and kilopascals (kPa). Median age, kPa, and CAP scores were compared using Wilcoxon rank sum test between groups.

Results: In our cohort of 1101 patients, the most common indications for Fibroscan® were HCV (324), HBV (285), NAFLD (298) and other (194). Groups with the highest kPa values were those with known cirrhosis, abnormal transaminases, HCV, followed by abnormal LFTs, Nonalcoholic Fatty Liver (NAFL), and Nonalcoholic steatohepatitis (NASH). The median age of patients referred for Fibroscan® for NAFLD was 60.19 vs. HBV or HCV at 57.51 (p<0.001). There was no significant difference between median kPa of NAFLD vs. HBV or HCV 5.8 vs. 5.5 respectively (p=0.22). Median CAP scores of NAFLD vs. HBV or HCV groups were 322 vs. 222 respectively (p<0.001).

Conclusions: Patients receiving Fibroscan® in Hawai‘i for NAFLD were significantly older than those with HBV or HCV. The kPa values were not statistically different in these two groups but CAP values were significantly higher patients with NAFLD. These findings indicate a bias towards earlier referral for HBV and HCV patients than NAFLD. Clinicians need to be educated on the severity of NAFLD in order to prevent progression to cirrhosis in these patients.
POSTER PRESENTATIONS
Introduction: Wheezing is a relatively common complaint in young adults and is often associated with asthma. The clinical history and physical exam are important in distinguishing asthma from alternative explanations for wheezing such as upper airway pathology. We present a case of a young female patient with Idiopathic Subglottic Stenosis who may otherwise have been incorrectly diagnosed with a common etiology had there not been high clinical suspicion for upper airway pathology.

Case: A 28-year-old previously healthy female presented with progressive exertional wheezing and dyspnea over the course of one year. Symptoms originally occurred only with strenuous exercise but by the time of referral were also noted with minimal exertion and with anxiety. Inspiratory and expiratory wheezing was audible and localized to the neck. Symptoms were alleviated by resting and relaxation. She denied any resting dyspnea, nocturnal symptoms, coughing, tightness, or wheezing in the chest. Prior to pulmonary referral the patient was tentatively diagnosed with exercise induced bronchospasm (an asthma variant). Initial spirometry was normal. Methacholine challenge testing, serial spirometry with exercise bronchoprovocation, and fiberoptic laryngoscopy revealed no clear diagnosis. However, the flow-volume loops of repeated spirometry efforts demonstrated an unusual pattern suggestive of a fixed large airway obstruction. The consulting pulmonologist requested a CT neck, which revealed a tracheal narrowing with a tracheal web 3 cm distal to the true vocal cords. Otorhinolaryngology evaluation revealed a bifurcated stenosis with lateral outpouching consistent with subglottic stenosis. Multimodal therapy with balloon dilation, laser lysis of adhesions, and mitomycin C relieved her symptoms and allowed a return to normal exercise. Symptoms gradually recurred, and annual follow-up evaluation revealed recurrent subglottic stenosis. This was again treated with dilation and lysis, pending definitive surgical intervention.

Discussion: Idiopathic subglottic stenosis is a rare disorder manifesting as subglottic stenosis without known causes such as recurrent intubation, relapsing polychondritis, or granulomatosis with polyangiitis. The disease is characterized by recurrent, circumferential inflammatory scarring resulting in stenosis. It occurs almost exclusively in women between aged 20-50 and frequently requires several endoscopic treatments followed by a definitive laryngo-tracheal resection. This patient was only correctly diagnosed due to a combination of clinical suspicion and persistence in evaluating for atypical causes of wheezing. Therapies for more common disorders such as asthma or vocal cord dysfunction would offer no benefit and potentially harm this patient. This case underscores the importance of expert clinicians’ intuition.
INTRODUCTION: Pulmonary artery intimal sarcomas (PAIS) are rare tumors and difficult to diagnose. We present a case of PAIS initially misdiagnosed as a pulmonary embolism (PE). Using a novel diagnostic approach - endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) – the patient was diagnosed with PAIS and referred for therapy.

CASE: An otherwise healthy 67-year-old woman presented to an outlying ER with 2 months of progressive dyspnea on exertion. She was mildly tachycardic, but physical examination was otherwise unremarkable. A D-dimer assay was negative. CTA of the chest revealed an impressive PE with near total occlusion of the right main pulmonary artery. Lower extremity ultrasound was negative for DVT. Hypercoagulable work up was unrevealing. An echocardiogram demonstrated normal LVEF, normal RV function & estimated PA systolic pressure (PASP) of 23 mmHg. At that time, she was given a diagnosis PE, treated with dabigatran and eventually referred to our clinic. After 3 months there was no improvement in dyspnea. Repeat CTA showed increased cross-sectional diameter of the endovascular process in the right main pulmonary artery (3.2 cm vs 2.1 cm) as well as proximal extension into the left main pulmonary artery. An endovascular tumor was suspected. Repeat echocardiogram now showed PASP 45 mmHg. PET scan demonstrated that the mass in the PA was intensely hypermetabolic (mSUV 21.4). EBUS-TBNA was performed to establish a diagnosis. An elongated echodense mass was found involving the entire right main PA as well as the proximal left main PA. Cytology from the mass was consistent with sarcoma. She was referred for palliative pulmonary artery tumor resection. Pathology confirmed a 10 cm PAIS. Her symptoms significantly improved after surgery. She attempted chemotherapy but discontinued due to side effects. Serial CT scans have shown local recurrence and progressive tumor burden in the right lung. Despite this, for many months she remained asymptomatic and independent. However, over a year since initial presentation, the patient has eventually transitioned to hospice care.

DISCUSSION: Pulmonary artery sarcoma poses a diagnostic challenge; surreptitious progression leaves the patient symptomless until advanced stages of disease. Mimicking other pulmonary vascular diseases contributes to delay in diagnosis. PAIS should be included in the differential of thromboembolic pulmonary disease and pulmonary hypertension. EBUS-TBNA offers a novel approach to the diagnosis of this rare condition. To date, there has been one published report of PAIS diagnosed using EBUS-TBNA. This approach carries some risk, however in the hands of an experienced operator can be a safe and less invasive alternative to percutaneous or surgical biopsy.
Thyrotoxicosis is often treated medically with anti-thyroid drug (ATD) therapy, including methimazole (MMI) and propylthiouracil (PTU), to inhibit the synthesis and release of thyroid hormones. An uncommon but potentially serious complication of ATDs is agranulocytosis, estimated to occur in around 0.2% of patients with Graves’ disease. Herein we describe two such cases. In our first case, a 30-year-old female with Graves’ disease previously lost to follow up was admitted for pyelonephritis that eventually resolved with one dose of cefepime and 7-day course of cefixime. However, due to signs of thyrotoxicosis on admission including tachycardia over 130 beats per minute, anxiety, exophthalmos, undetectable TSH, and mildly elevated free T4 and T3, she was started on both MMI and PTU. Her white blood count, which had been normal on admission, dropped to a nadir of 3100 cells/mm3 on hospital day 3. ATD therapy was then stopped, and her white blood count normalized within 6 days. Her thyrotoxic symptoms were controlled by propranolol and saturated solutions of potassium iodide (SSKI) until she could receive total thyroidectomy. In our second case, a 25-year-old active duty female with Graves’ disease developed pharyngitis 3 weeks after starting MMI. She was found at that time to have an absolute neutrophil count of 5 cells/mm3, undetectable TSH, and mildly elevated free T4. MMI was stopped, she was treated for neutropenic fever with cefepime and filgrastim until resolution of neutropenia, and her hyperthyroidism was treated with SSKI, cholestyramine, and propranolol. Her WBC and free T4 normalized within 4 days of presentation. Due to a prior fine needle aspiration biopsy of a thyroid nodule with atypical cytology, she received a total thyroidectomy for definitive treatment of Graves’ disease, pathology of which confirmed pT1a papillary thyroid cancer. These cases reinforce that agranulocytosis is a potentially life-threatening complication of ATDs of which all prescribers and patients need to aware. Treatment requires immediate suspension of the offending agent, and a multimodal pharmacological approach can achieve euthyroid state to successfully prepare patients for definitive treatment.
RARE ANAPHYLACTIC REACTION TO ACAMPROSATE IN A YOUNG ALCOHOLIC

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Introduction: Alcoholism is a serious health issue in Hawai‘i with 22.3% of the adult population drinking alcohol to excess, well above the national average of 18%. The state reports the fifth highest rate in the United States of driving deaths related to alcohol. Effective alcohol abuse treatment programs, which combine therapy with medications, are necessary to provide the appropriate care that the citizens of Hawai‘i need. When it comes to medical management our options are Naltrexone, Acamprosate, or Disulfiram. Due to poor compliance, Disulfiram is only used as a second line agent. These medications play an integral role in the treatment of alcohol abuse and it is necessary for healthcare providers to be aware of their side effect profiles. This includes a rare and fatal anaphylactic reaction to Acamprosate which is not well documented in the literature.

Case Report: A 32-year-old homeless gentleman with a history of chronic alcohol abuse, has been abstinent for two months, and recently started on Acamprosate. He is living in a shelter with his girlfriend who had just recovered from an infection of her bilateral axilla. He used his girlfriend’s deodorant and subsequently developed large, painful boils under his right axilla and groin simultaneously. After taking a warm bath he self-lanced both boils which lead to the development of fatigue, muscle aches, pains, and low-grade fevers. Later that night he took Acamprosate with an energy drink. Shortly after taking his medication he developed severe urticaria and pruritis. He went to bed and the next morning developed significant angioedema of the bottom lip. The patient went to an urgent care center, was treated with Prednisone, and had a nasal swab for influenza which was positive. He was treated with Tamiflu and sent home. He went on to develop significant angioedema of the upper lip prompting him to go to the emergency room. The Acamprosate was immediately discontinued and the patient was informed to never take this medication again. He was treated with steroids and Benadryl with gradual improvement of symptoms until complete resolution.

Discussion: Hypersensitivity reactions to Acamprosate including urticaria, angioedema, and anaphylaxis are rare and not well documented in the literature but do occur. Patients dealing with alcohol abuse tend to have complicated histories with multiple comorbid conditions which can make it difficult to identify the source of these symptoms. Missing this diagnosis will have dangerous consequences for patients and can lead to death. With alcohol abuse being so prevalent in Hawai‘i, local healthcare providers who are using this medication need to be well educated and made aware of this serious reaction.
A CASE OF MYOEPITHELIAL CARCINOMA WITH DIFFUSE METASTASIS: AN UNUSUAL PRESENTATION OF A RARE MALIGNANCY

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Introduction: Myoepithelial carcinoma is made up of myoepithelial cells which display a dual epithelial and smooth muscle phenotype. The incidence has been reported as 0.2% of malignant salivary gland tumors, which rare (0.9 cases per 100,000). They arise from a malignant transformation of a benign pleomorphic adenoma or a benign myoepithelioma. These tumors originate from the parotid glands (66%) followed by minor salivary glands and submandibular gland. They are diagnosed at the average age of 55 years though there are reports as early as age 16. These tumors present as a rapidly increasing painless mass. Distant metastases of this carcinoma has been noted in the lungs, bone, kidneys, and brain. Microscopic findings of these carcinomas are described as unencapsulated and multinodular in appearance with infiltrative borders. Useful immunohistochemical markers include cytokeratins (AE1/AE3), Vimentin, S-100, Calponin, SMA, MSA, smooth muscle myosin, P63 protein, GFAP, and CD10.

Case Report: A 31 year old female with past medical history of degenerating fibroids and asthma, presented for flu-like symptoms and 3 months of chronic cough, palpititations, blood-tinged-sputum, and back pain. Imaging revealed pulmonary nodules in the bilateral lungs, mediastinal lymphadenopathy, and soft tissue masses in the lumbar spine. Pulmonology suggested IR guided biopsy, which resulted in myoepithelial carcinoma of plasmacytoid appearance, positive for CK AE1AE3, SMA, Desmin, and focally for S100. Oncology planned for Foundation One testing and CAP cisplatin/doxorubicin/Cytoxan treatment and radiation. Unfortunately, the patient arrested out of hospital, and spontaneous circulation was restored after 10 minutes of CPR. The patient was intubated and mechanically ventilated. MRI Brain revealed acute infarcts throughout both hemispheres and diffuse leptomeningeal enhancement which could be carcinomatosis. Echocardiogram revealed two cardiac masses over 1 cm in greatest dimension which Cardiology felt were more consistent with tumor rather than thrombus or vegetation. EEG confirmed severe encephalopathy and repeat MRI were compatible with extensive anoxic brain injury.

Conclusion: Myoepithelial Carcinomas are difficult to diagnose, and complications are difficult to anticipate. The problem extends from 1) its rarity, 2) variability in clinical presentation, and 3) variability in morphological arrangement and histologic patterns. Our patient’s presentation with cardiac arrest may be due to cardiac metastasis which is extremely rare, with one case published in 2016. Immunohistochemical analysis was crucial for diagnosis. No clear management strategy has been established for this malignancy. Surgery is limited to resecting the primary mass only and radiotherapy and adjuvant chemotherapy provide unclear benefits. Myoepithelial Carcinomas bear an unclear prognosis and are feared for its variability of presentation, unpredictable behavior, tendency for distant metastases, and unproven treatment strategy.
In the US, overall cancer incidence and death rates have both declined steadily in recent decades. However, liver cancer remains a significant outlier, with the incidence of liver cancer in the US having increased 72 percent between 2003 and 2012 [1]. Within the United States, Hawai’i has an especially high incidence of liver cancer. In 2016, age-adjusted death rates for liver cancer in our state were the third highest in the country [2].

To our knowledge there are no published data describing patients with a history of hepatitis C (HCV) infection who develop hepatocellular carcinoma (HCC) in Hawai’i. Our goal is to better understanding the interplay between hepatitis C and HCC, with an eye to the development of predictive tools for earlier liver cancer diagnosis.

**Methods:** Our study is a retrospective review of patient data from both Health Connect—the electronic medical record used for all Kaiser Permanente Hawai’i (KPHI) members since 2004—as well as a separate database of patients with hepatitis C infection maintained by KPHI’s Viral Hepatitis Clinic at Moanalua Medical Center. The study cohort included all patients in these databases from 2004 to the present (2018) who met criteria for both hepatitis C infection (current or cured) and hepatocellular carcinoma.

**Results:** Our patient cohort was disproportionately male (76%) and when compared to the general population more likely to have a history of smoking (13.1% vs 21.8%) or diabetes (10.9% vs 29.1%). Compared to patients with Hep C infection who did not develop HCC, male gender, genotype 3 hep C infection, and hep B core antibody positivity were all significantly more common in our cohort (p < 0.05). Median platelet level was 114 K/uL and median alpha-fetoprotein level was 52 ng/ml. Majority of patients with no transplant or resection lived < 1 year (48.7%) while majority of patients with transplant or resection lived >5 years (46.7%).

**Discussion:** Our retrospective study suggests several factors of potential importance in the development of a predictive model for liver cancer in patients from Hawai’i with a history of Hep C infection: male gender, diabetes, smoking history, genotype 3 HCV infection, hep B exposure, thrombocytopenia, and alpha-fetoprotein level are possible targets for predictive modeling. Such a model might allow for more aggressive liver cancer screening for selected patients with a history of hepatitis C, in hopes of achieving earlier HCC detection and improved long term survival.
TAKOTSUBO CARDIOMYOPATHY IN HAWAI‘I

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Introduction: Takotsubo Cardiomyopathy is a syndrome that mimics acute coronary syndrome that has been described globally. Patients often present with chest pain, abnormal EKGs and biomarkers suggestive of myocardial injury. However, its incidence, clinical characteristics and outcomes, specifically in Hawai‘i, has not been fully evaluated. In our study, we will identify Takotsubo patients in the Kaiser Hawai‘i population and gather demographic and objective data. This information will be analyzed for similarities and possible trends with comparison of the data to those found in literature.

Methods: We looked at patients in the KP Hawai‘i system with a diagnosis of Takotsubo Cardiomyopathy between 2008-2010 with 142 patients identified; preliminary data of 50 patients shown. Electronic medical records were used to retrospectively review patient demographics and medical history, presentation upon hospital admission, imaging and lab findings, medications and outcome. The study population does not include vulnerable populations or have any specific subject exclusion criteria.

Results: Age Range (33-91), Sex (M 7,F 43), Ethnicity (Native Hawaiian 12, Filipino 3, Chinese 1, Japanese 6, Caucasian 22, Other 6), Psychiatric History (Yes 9, No 39), Triggers (Emotional 14, Physical 17, Both 2, Unknown 15), Trigger Time (Morning 9, Afternoon 2, Evening 8), Presenting symptoms (Chest Pain 30, SOB 17, Other 15), Admitting Diagnosis (ACS 37, CHF 3, Other 12), EKG (STE 4, STD 2, TWI 19, NSST 9, NLBBB 1, Other 1), Avg Trop (4.9), Avg Cardiac Echo (EF 35%), LV Thrombus (Yes 1, No 32), WMA (Apical 27, Mid 23, Base 1, Other 7), Hospital Complications (Cardiac Shock 16%), Discharge Medications (BB 41, ACE 19, ARB 6, CCB 3, Loop Diuretic 10, Aldactone 3, Follow-up (Avg Time 71 Cardiac EF Avg 53%), Mortality (Deceased 6)

Conclusion: Our demographics show higher incidence in older, female and Caucasian patient populations. Emotional and physical stress seemingly triggers the event with chest pain as the most common complaint. Common EKG findings of T-wave abnormalities and non-specific ST changes. Apical and mid cardiac wall motion abnormalities most common on transthoracic echocardiogram. Most common hospital complication was cardiogenic shock. Recommend heart failure medications with beta blocker and ACE inhibitor at discharge.1 Average time of repeat cardiac echo in our study was around two months with improvement of ejection fraction. Consider physical and/or emotional stress management. Literature indicates prognosis of these patients are not benign with any cause death rate of 5.6% per patient year and cardiac and cerebrovascular events of 9.8% per patient year3.
HANDGRIP STRENGTH IN LATE LIFE PREDICTS FUTURE FUNCTIONAL IMPAIRMENT: THE KUAKINI HONOLULU-ASIA AGING STUDY

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Background: Grip strength in midlife has been shown to predict future disability and functional limitation, but few studies have examined this relationship in late life. Our objective was to study whether grip strength in functionally intact older men predicted future functional impairment over ten years of follow-up.

Methods: The Kuakini Honolulu Heart Program (HHP) is a longitudinal cohort study of Japanese-American men since 1965. The Kuakini Honolulu-Asia Aging Study started with HHP exam 4 (1991-93), when 3,741 men ages 71-93 years participated. Functional impairment was defined as any impairment in at least one of the following categories: self-reported ADLs, measured walk speed <0.4 m/s, or inability to do a single chair stand. Handgrip strength was measured using a handheld dynamometer. We excluded those with functional impairment at baseline, leaving an analytic sample of 1,381 men. We compared development of new functional impairment over 3, 6 and 10 years, by tertiles of handgrip strength using multiple logistic regression, adjusting for baseline age, height, weight, education, physical activity, pack-years smoking, prevalent chronic diseases and cognitive impairment.

Results: Weaker tertiles of handgrip strength predicted incident functional impairment at 3 years (42.6% vs. 35.3% vs. 28.7%, p<0.0001), 6 years (59.7% vs. 47.4% vs. 40.6%, p<0.0001) and 10 years (58.7% vs. 54.4% vs. 41.3%, p=0.0001). After adjusting for all factors and using the strongest tertile as reference, grip strength was associated with incident functional impairment at 3 years (weakest tertile OR=1.72, 95% CI=1.27-2.34, p=0.0005; middle tertile OR=1.43, 95% CI=1.08-1.88, p=0.01), 6 years (weakest tertile OR=2.11, 95% CI 1.52-2.92, p<0.0001; middle tertile OR=1.35, 95% CI=1.02-1.79, p=0.03), and 10 years (weakest tertile OR=1.68, 95% CI=1.10-2.56, p=0.02; middle tertile OR=1.55, 95% CI=1.08-2.23, p=0.02).

Conclusions: In elderly Japanese-American men with no functional disability at baseline, weaker handgrip strength was an independent predictor of future functional impairment. Measurement of grip strength in the oldest old may assist clinicians to identify patients at higher risk of functional decline and provide patients and caregivers with anticipatory guidance.

Funding Sources: Kuakini Medical Center, National Institute on Aging (NIA), National Heart, Lung and Blood Institute (NHLBI), and the Veterans Affairs Pacific Islands Health Care System (VA).
WHEN ANTITERRORISM HURTS THE HEART: A CASE OF MYOCARDITIS IN AN ACTIVE DUTY SOLDIER SECONDARY TO PRESUMED SMALLPOX VACCINE ADMIN

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Introduction: Since 2002, more than 2 million United States military members have undergone vaccination against smallpox. Smallpox, a disease caused by the Variola virus and notorious for its high mortality rate, was eradicated in 1977 such that most modern-day Americans are unfamiliar with this disease nor have exposure to the vaccine. However, due to concern over the growing threat of bioterrorism, the military population remains with an extensive smallpox vaccination program. Like most medical interventions, vaccinations are not without risk. Here we present a case of an active duty soldier who developed myocarditis following administration of the smallpox vaccine.

Case Presentation: A 24-year-old active duty soldier with an unremarkable medical history presented to a tertiary emergency department after experiencing acute onset of chest pain while at rest. The pain was described as centrally located and burning in quality, associated with nausea and shortness of breath. An electrocardiogram was performed; significant for ST elevation in leads II, III, aVF, IV, V, and VI. Labs were significant for an elevated troponin (7.58). A heparin drip was initiated, and the soldier was immediately transferred to a facility capable of cardiac catheterization; thrombolytics were deferred at that time. Cardiac catheterization was without obstructive disease. A subsequent echocardiogram and cardiac magnetic resonance imaging (cardiac MRI) demonstrated normal coronary artery anatomy, an estimated ejection fraction of 50-55%, and normal chambers with no wall thickness. The soldier was treated symptomatically; counselled to avoid strenuous activity and alcohol. And subsequently discharged home with close follow-up. Four months later, repeat echocardiogram showed a normalized ejection fraction, 60-65%. Prior to returning to regular activity, an exercise treadmill test was performed, the soldier was deemed low risk with a Duke Score of 9 and able to return to normal activities.

Discussion: Myocarditis, or inflammation of the myocardium, is a rare but a known side effect of the smallpox vaccine. It commonly presents 2-29 days, with the average of 10 days, post immunization. Signs and symptoms of myocarditis are nonspecific but may mimic acute coronary syndrome or heart failure. Work-up includes blood tests including cardiac biomarkers, with invasive and noninvasive imaging. Electrocardiogram findings may demonstrate ST abnormalities. Once acute causes chest pain and discomfort are ruled out, if clinical suspicion remains high, the gold standard to diagnosis myocarditis is an endomyocardial biopsy. The condition is self-limiting and includes symptomatic care with counseling to reduce exercise and consumption of alcohol. Given the population of Hawai’i is approximately 4% active duty military personnel and the fourth-largest military work force in the nation is located on Oahu, it is imperative that Hawai’i-based providers recognize myocarditis as a potential adverse reaction to the smallpox vaccine.
The treatment of acute myocardial infarction (MI) involves reestablishing blood flow (reperfusion) to the heart to rescue cardiomyocytes from ischemia. However, reperfusion injury remains to be an important contributor to the development of adverse remodeling post-ischemia, increasing mortality in MI patients. Clinical studies indicate that residual iron (Fe) within the infarct zone post-MI is associated with adverse remodeling. Ferroptosis is a recently discovered form of regulated cell death involving cellular iron (Fe) and lipid reactive-oxygen species (ROS) generation. In addition to ferroptosis, mitochondrial Fe has been shown to increase in the cardiomyocyte after ischemia-reperfusion (I/R) injury, likely contributing to the formation of lipid ROS and consequent cell damage. A previous study reported that in ex vivo I/R injury models, treatment with Fe-chelator deferoxime (DFO) preserved cardiac function by inhibition of ferroptosis. However, we did not observe the cardioprotective effects of DFO in the same model, while ferrostatin-1, a ferroptosis inhibitor, restored recovery of ventricular contraction following short ischemia. We anticipated the discrepancy between the two independent experiments was caused by the level of Fe in the circulating buffer. To determine the pathophysiological effects of extracellular Fe in I/R injury, we assessed the role of supplemental Fe in perfusate in ex vivo I/R injury models. Adult male wild-type mice were subjected to ex vivo global I/R (20 min ischemia, 40 min reperfusion) as done previously. The hearts were perfused with 10mM of Fe (III)-citrate (n=2), 1mM of Fe (III)-citrate (n=3), 80μM of DFO (n=5), 80μM of DFO plus 1mM of Fe (III)-citrate (n=3), or control buffer (n=8) during the initial equilibration period, and assessed recovery of left ventricular developed pressure (LVDP) at reperfusion. One of the hearts perfused with 10mM of Fe (III)-citrate did not recover at all and another heart with the same treatment recovered less than 10%. On the other hand, the percent recovery in hearts treated with 1mM of Fe (III)-citrate was comparable to that in control hearts (22.98 ± 8.30% vs. 21.53 ± 1.93%, n.s.). These findings suggest that excess Fe during I/R exaggerated cardiac dysfunction in I/R injury. Although groups perfused with DFO or DFO plus 1mM of Fe (III)-citrate recovered better than control hearts (27.28 ± 4.26% and 27.62 ± 7.75%), they were no statistically different from the control. These findings suggest that circulating Fe is a key pathophysiological factor in mediating I/R injury and that Fe-chelation may protect the heart when ferroptosis is activated. However, further studies are necessary to conclude the effects of Fe-chelators in I/R injury.
While iron is essential for many biological functions, excess iron has potentially toxic aspects. Clinical studies suggested that the presence of myocardial hemorrhage in post-myocardial infarction (MI), which was associated with residual myocardial iron, is a risk for adverse left ventricular (LV) remodeling and heart failure. Our group recently demonstrated that the overexpression of mTOR (the Mammalian Target of Rapamycin) is necessary and sufficient for protecting cardiomyocytes (CM) against excess iron in CMs isolated genetic mouse models. However, direct manipulation of mTOR in adult CMs is technically difficult due to the large size of the mTOR protein (280 kDa). Telomere maintenance 2 (Tel2) is known as the stabilizing protein of phosphatidylinositol 3-kinase-related protein kinases (PIKKs) such as mTOR. The molecular size of Tel2 is reasonable for generating recombinant viruses (91 kDa). Previously we reported the protective effects of Tel2 in H9ce cells, rat ventricular myoblast cell lines, but not in adult CMs. In this study, we examined whether Tel2 is sufficient to prevent cell death against excess iron in adult CM. Mouse adult CMs were isolated from hearts of mice at 12–20 weeks of age, and cultured in a 12-well plate with conditioned medium (Medium 199, 100 μg/ml bovine serum albumin, insulin-transferrin-sodium selenite, 25 μM blebbistatin, 100 U/ml penicillin, 100 μg/ml streptomycin) as done previously. Immediately after plating, CMs were infected with 5 μL of 1x109 particles (pt)/ml of adenovirus carrying Tel2 (Ad-Tel2) or 5 μL of 1x109 particles (pt)/ml of control virus (Ad-GFP). One day after infection, we confirmed adenoviral gene transfer in CMs infected with Ad-GFP and Ad-Tel2 with green fluorescence. After that, CMs were treated with 10 mM of Fe (III)-citrate for 18 hours. Cell viability was assessed by Live/Dead Cell Viability Assay (2 μM calcein AM for survival, and 4 μM ethidium homodimer-1 for cell death). Control virus (Ad- GFP) did not significantly change cell survival in excess iron-treated CMs (cell death %; 72.8±5.1% vs. 69.4±7.1%, no infection vs. Ad-GFP, n=10-12). Although there was no statistically different, there is some tendency in cardioprotective effects of Tel2 overexpression by Ad-Tel2 in CM cell survival against excess iron (cell death %; 64.3±5.6%, n=12). Further studies are required to define the role of Tel2 in protecting adult CMs against excess iron. Understanding the role of mTOR-binding protein, Tel2, in preventing iron-mediated cell death could provide novel target for a therapy of heart failure following MI in the future.
Mitral annular calcification (MAC) is a common valve finding that rarely progresses to mitral stenosis (MS).

A 75-year-old Filipino female, with a past medical history of congestive heart failure, atrial fibrillation, diabetes mellitus type 2, hypertension, right middle cerebral artery stroke with left hemiparesis in 2010, seizure, and multiple ICU admissions for sepsis secondary to pneumonia with hemoptysis, who presented with acute respiratory failure. Home medications include digoxin, metoprolol tartrate, and warfarin. She became unresponsive while on CPAP with desaturation requiring intubation. Physical exam was significant for irregularly irregular rhythm, diastolic rumble, rales, and rhonchi. Chest x-ray: mild cardiomegaly, MAC, calcified thoracic aorta, pulmonary congestion and infiltrates. EKG: atrial fibrillation with rate averaging 107. A 2016 Echocardiogram in atrial fibrillation: left ventricular ejection fraction 55 – 60%, moderately dilated left atrium, severe calcification of the anterior mitral valve leaflet, moderate thickening and calcification of the posterior mitral valve leaflet and MAC, moderate-to-severe MS with mitral valve area (MVA) of 1.2 cm² by pressure ½ time, right ventricular systolic pressure of 41.79 mm Hg. Significant changes noted in 2018 echocardiogram included MVA of 1.4 cm², increased left atrial enlargement, right ventricular systolic pressure of 72.62 mm Hg. Haemophilus influenzae pneumonia was diagnosed. Transesophageal echocardiography: moderate mitral stenosis with MVA 1.4 cm². Cardiac catheterization: MVA by Gorlin’s 3.1 cm², cardiac output 3.3/min, and pulmonary artery pressures of 38/11 with a mean of 23 mmHg. There was no significant obstructive coronary disease.

This case illustrates an interesting change in MS etiology and thus management. Rheumatic heart disease has and still is the most common cause of MS but the incidence has decreased due to appropriate prevention and treatment of rheumatic fever in the United States. Most cases of mitral stenosis are discovered in immigrants. MAC is age-related and as the population ages should become more prevalent. Dialysis patients are also increasing and with their altered calcium metabolism have more calcification. MS-related to MAC is increasing in incidence and may become a larger percentage of the MS patients. Balloon mitral valvuloplasty is the primary treatment for MS though would not be suitable for MS due to MAC. Echocardiography may underestimate the degree of MS. But the experience of one of the authors is that it overestimates the degree of MS. MAC-mediated MS can still lead to atrial fibrillation, pulmonary hypertension, recurrent lung infections, and congestive heart failure. This shift in MS pathophysiology may affect management considerations. The use of novel oral anticoagulants is contraindicated in valvular atrial fibrillation and balloon valvuloplasty is contraindicated in MS with severe calcification so mitral valve replacement may be necessary in severe cases.
Geriatric Syndromes and Inflammation in Older HIV-Infected Adults with Cognitive Impairment

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Background: Nearly half of the HIV-infected population in the US is now older than fifty years of age with at least 6% over the age of 65. Between 35-50% live with mild to moderate cognitive impairment. Older HIV-infected adults also have a substantial burden of non-AIDS medical conditions (HANA) and are at risk for frailty, geriatric syndromes, and early mortality compared to HIV-uninfected peers. We sought to define the magnitude of geriatric conditions and multimorbidity in HIV-infected adults over age 60 who are living with symptomatic cognitive impairment. In a subset of participants, we examine associations between these geriatric conditions and inflammation.

Methods: We recruited 141 participants from the HIV Elders Study at UCSF between 2013 and 2017 who were HIV-infected, virally suppressed, 60 years or older, and clinically diagnosed with Mild Neurocognitive Disorder (MND). We conducted standardized assessment of geriatric conditions and everyday function and investigated multimorbidity burden using the Veterans Aging Cohort Study (VACS) index.

Results: Among HIV-infected older adults with MND 58% report incontinence, 55% meet criteria for pre-frailty, and a substantial proportion report dependence with iADLs (52%) or ADLs (41%). The mean (SD) VACS Index score is 33 (14), suggesting a 13.8% 5-year all-cause mortality risk. Among geriatric conditions examined, the VACS index associates with neopterin, a marker of monocyte activation (p<0.010). No associations were found between neopterin or soluble (s) CD163 and other geriatric conditions.

Conclusions: HIV-infected older adults with symptomatic cognitive impairment carry a substantial burden of other geriatric conditions. Our work supports the need for comprehensive geriatric systems of care for cognitively impaired individuals aging with HIV.
CHARACTERIZING PATTERNS OF LIPID REACTIVE OXYGENE SPECIES-INDUCED CELL DEATH OF IN VITRO CARDIOMYOCYTES

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Newer treatments of myocardial infarction (MI), like coronary stents and bypass grafts, have led to a better prognosis for patients. However, heart failure (HF) following MI remains a major contributor to morbidity and mortality. The risk of future HF is directly correlated to the magnitude of cardiomyocyte (CM) cell death caused by acute MI. We and other groups have previously reported the cell-to-cell death propagation of CMs in hypoxic hypercontracture observed in I/R injury. Recently, we reported that ferroptosis, which is triggered by accumulation of lipid reactive oxygen species (ROS), is a significant type of cell death in isolated adult CMs using the class 1 and class 2 ferroptosis inducers, elastin and Ras-selective-lethal 3 (RSL3) respectively. RSL3 induces ferroptosis directly by inhibiting the phospholipid hydroperoxidase glutathione peroxidase 4 (GPX4) that suppresses the damage caused by lipid reactive oxygen species. However, cell-to-cell death propagation with RSL3 has not yet been characterized. To determine the characteristics of RSL3-induced cell death, we assessed the effects of RSL3 in cell-to-cell death propagation using gel-induced focal cell death in cultured CM.

We cultured H9c2 cells, originally derived from embryonic rat ventricles, in 40 mm dishes containing DMEM with 10% FBS. Cells were cultured to about 90% confluency and the experimental groups were pre-treated with 1 micromol/L RSL3 for 2 hours. An acidic cylindrical gel (pH = 6.2) was then placed in the center of the dish to induce local CM cell death via acidosis and hypoxia, where are observed in I/R injury in vivo. Five hours after placing the gel, necrotic cell death was evaluated using Evans Blue (EB) stain. We observed RSL3 treatment-enhanced cell-to-cell death shown by a blue line extending from the dead cells under the gel to the peripheral cells compared to non-treated cells.

These findings suggest that the inhibition of the protective GPX4 system by RSL3 exaggerated cell-to-cell death propagation in CM. A better understanding of this unique cell-to-cell propagation of CM cell death will lead to better treatment and prevention of I/R injury following an acute MI.
STERCORAL COLITIS, A SERIOUS AND FORGOTTEN CASE OF SEPSIS

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Stercoral colitis with subsequent ischemic colitis is a rare and potentially fatal outcome of chronic constipation and fecal impaction. We present a patient with chronic immobility, who was prescribed agents with potential for bowel dysregulation and who progressed to a surgical abdomen.

A chronically immobile 69-year-old man presented to the ED with abdominal pain and confusion. He was in his usual state of health with end stage renal failure on hemodialysis and chronic atrial fibrillation, until 1 week prior to admission when he developed constipation. Among his medications were sevelamer carbonate and calcium. 8 hours prior to admission, the patient awoke with diffuse abdominal pain, nausea, non-bilious, non-bloody emesis and non-bloody, non-mucoid, non-melenic loose stools. His family stated that he had not complained of fever, chills, chest pain, dyspnea, or cough. The physical exam was remarkable for a BP of 75/48, respiration 27 breaths/min, altered mental status, irregularly irregular cardiac rhythm, diffuse abdominal pain with moderate distention, and hypoactive bowel sounds. Laboratory studies revealed WBC 13.1, Hgb 9.5, lactate 6.2 mmol/L, BUN 60 mg/dl, Creat 5.7 mg/dl, normal LFT, electrolytes. Abdominal x-ray revealed moderate to large amount of stool in the lower sigmoid colon and rectum. CT KUB revealed distended loops of bowel with scattered gas liquid levels without definite transition point, markedly distended sigmoid colon and rectum with dense stool, and moderate wall thickening. He was initially treated with broad spectrum antibiotics and bowel regimens to induce defecation. Abdominal x-rays revealed unchanged stool burden. Digital disimpaction was unsuccessful. He was taken to surgery on day 8 of hospitalization, underwent sigmoidoscopy and was found to have a severely ischemic and thickened sigmoid colon. He underwent exploratory laparotomy which revealed significant necrosis of the sigmoid colon with large amounts of fibrinous exudate, prompting sigmoidectomy with end colostomy and Hartmann’s Pouch.

Fewer than 200 cases of stercoral colitis have been reported in the literature. Only 3 case reports and 2 case series of stercoral colitis with ischemic colitis and lactic acidosis have been reported in total. The disease is rapidly progressive and typically affects patients who are bed-bound, geriatric, with neuropsychiatric or cognitive conditions, or on medications that hinder gastrointestinal movement. Prevention requires insightful physician care. A high index of suspicion is necessary for a rapid diagnosis and prompt initiation of intervention to avoid ischemic complications. Mortality is estimated at over 30%. This patient reflects the complexities involved in diagnosing and managing stercoral colitis. Physicians should consider the diagnosis early and determine whether their patient would benefit from early endoscopic disimpaction to avoid the serious sequelae of this pathology.
EOSINOPHILIC EXPLOSION: A CASE OF UNRELENTING SUBSEROAL EOSINOPHILIC GASTROENTERITIS

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Introduction: Eosinophilic gastroenteritis (EGE) is a rare condition characterized by peripheral eosinophilia and eosinophilic infiltration of the gastrointestinal (GI) tract. Patients present with non-specific GI symptoms. There are 3 types: mucosal, muscularis, and subserosal. The latter is the rarest and most severe variant, characterized by eosinophil-rich ascites. Early corticosteroid therapy typically results in favorable outcomes. Here, we present a unique case of subserosal EGE with quick relapse after steroid discontinuation.

Case: A 33-year-old obese woman with allergic rhinitis was admitted with a week-long history of intractable nausea, non-bloody diarrhea, diffuse abdominal pain, and distention. Past surgical history included gastric banding and cholecystectomy due to gallstones. Notably, one month prior to admission the patient developed heartburn and regurgitation, at which time esophagogastroduodenoscopy (EGD) with biopsy demonstrated eosinophilic esophagitis. Testing for H. pylori was negative, and she was started on daily proton-pump inhibitor. Inpatient abdominal examination revealed mild distention, diffuse tenderness, and positive fluid wave. Contrast-enhanced abdominal computed tomography (CT) showed ascites, mesenteric lymphadenopathy, and widespread thickening of the mid-to-distal esophagus, distal stomach, and colon, as well as small bowel wall with “target” pattern of enhancement. Laboratory examination revealed leukocyte count 19,600 with 39% eosinophils. Liver function tests, C-reactive protein, erythrocyte sedimentation rate, prothrombin time, partial thromboplastin time, anti-neutrophil cytoplasmic antibodies, and anti-nuclear antibody were normal. Immunoglobulin E was elevated three-times the upper limit of normal. Stool polymerase chain reaction to test bacterial, viral, and parasitic pathogens was negative. Diagnostic paracentesis demonstrated sterile ascitic fluid, no malignant cells, and leukocyte count 3658 with 72% eosinophils. EGD showed moderate erythema of the gastric antrum and second portion of the duodenum. Histology re-demonstrated eosinophilic esophagitis, gastric and duodenal biopsies did not reveal cellular infiltration. The patient was treated with prednisone for subserosal EGE with profound symptomatic improvement. Less than 2-months after completion of her steroid course, her symptoms returned. Labs again showed severe peripheral eosinophilic leukocytosis. Repeat CT abdomen showed findings similar to her prior admission. The patient was provided another course of prednisone, and has since been in remission.

Discussion: A high-index of suspicion for subserosal EGE is essential in patients presenting with peripheral eosinophilia and new-onset ascites. The diagnosis is often challenging because biopsies obtained during EGD are often limited to the mucosal layer and fail to sample the deeper, affected subserosal layer. Ascitic fluid revealing prominent eosinophilia is therefore key to recognizing the subserosal type. Oral steroid therapy is first-line treatment and can yield a dramatic response. Steroid-sparing therapy may be considered in difficult cases of relapse and unremitting EGE.
THE VERSATILITY AND STEALTH OF KLEBSIELLA PNEUMONIAE

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Introduction: Klebsiella pneumoniae is found in the normal flora of the gastrointestinal tract and is associated with both nosocomial and community acquired infections. Klebsiella can commonly cause pneumonia, empyema, and cystitis. However, more virulent strains can cause community-acquired primary invasive liver abscess syndrome, which can lead to metastatic infections at other sites including the eye and brain.

Case Presentation: A 50-year-old man with no medical history presented with symptoms of left eye pain, blurry vision and worsening pain, photophobia, and visual loss since the previous morning. A clinical diagnosis of acute fibrinous iritis was made by ophthalmology which was treated with oral and topical steroids and topical anticholinergic drops. He returned a few days later with worsening symptoms and was found to have panuveitis with concern for Wegener’s granulomatosis and toxoplasmosis. He was referred to rheumatology and given a course of oral antibiotics. A week later, he presented to the ED with complete visual loss of the left eye and was found to have a hypopyon and endophthalmitis. He underwent pars plana vitrectomy with anterior chamber washout and received intravitreal antibiotics. Vitreous and urine cultures returned positive for Klebsiella pneumoniae. Blood cultures were negative x2. An infectious disease consult was obtained. As he did not have any history of antecedent illness or ocular trauma, search of an endogenous source was pursued. A hyperechoic circumscribed lesion measuring 2.6 cm was seen on US in the right lobe of the liver which was confirmed by CT to be an abscess. Further imaging also identified several smaller lesions in the liver and a heterogeneous 3.5 cm lesion in the lateral cortex of the left kidney. The liver abscesses were too small to undergo percutaneous drainage. The patient was started on IV antibiotics. As a result of his workup, he was newly diagnosed with uncontrolled type 2 diabetes mellitus with a Hemoglobin-A1c of 10.1% and was started on insulin. He was discharged from the hospital with plans for a prolonged course of IV antibiotics. However, he represented 2 days after discharge to the ED with increased drainage from left eye. He was diagnosed with pre- and postseptal orbital cellulitis with abscess and was also found to have CT findings consistent with globe rupture. He eventually underwent washout and enucleation.

Conclusion: This case illustrates an interesting presentation of endogenous endophthalmitis in a patient with previously undiagnosed diabetes and metastatic community-acquired Klebsiella pneumonia infection. Klebsiella pneumoniae infection should be considered in patients with endophthalmitis especially in those that are immunocompromised.
SUCCESSFUL AGING: THE STUDY OF FRAILTY IN KAISER PERMANENTE HAWAI‘I KAI CLINIC SENIORS USING THE FRAIL SCALE

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Introduction: Frailty is a common geriatric syndrome characterized by a decline in physiological reserves, increased vulnerability to acute illness and stressors and increased risk for adverse outcomes such as falls, delirium, procedural complications, disability and death. Early recognition of frailty provides an opportunity for upstream primary care based interventions that can delay development of disability by promoting physically activity, nutrition, home safety, de-prescribing to avoid polypharmacy and advance care planning. The FRAIL scale is an internationally validated, interview based, copyright free screening test. Since 2016, it has been promulgated by St. Louis University as part of its “Rapid Geriatric Assessment”, a tool for primary care that can be administered by a variety of health care professionals.

Objectives: 1. To test the FRAIL scale as a population wide screening tool independent of individual face to face encounters using email, phone, letter and chart review with family or caregiver contact. 2. To screen the Kaiser Hawai‘i Kai (HAK) population ≥ 65 years old for frailty using the FRAIL scale via email, phone, letter and chart review.

Methods: FRAIL scale was sent by email three times, by letter for those =/>75 years old, by phone for those 65-74 years old. For those unable to answer, the FRAIL scale was completed by MD chart review and phone contact to family or caregivers. MD chart review was performed to ensure accuracy of response if > 5 illnesses were present.

Results: Of 1,406 HAK seniors contacted, the response rate was 79% with a predominance of non-responders in the 65-79 age range, due to time and resource limitations. After batched emails, the outreach method for the 65-74 year old group consisted of one time phone calls during Kaiser office hours, while letters, which yielded a higher return rate, were sent to persons 75 years and older. The HAK senior population was screened as 39% Robust, 29% Pre-Frail, 11% Frail, and 21% Non-Responders. As HAK seniors move from robust to frail, the percentage female appears to increase. This could suggest that females are at higher risk or contrarily that men are dying earlier.

Conclusions: We began with a search for a definition and a tool that could empower primary care physicians to identify persons at risk. Our journey led to a more personal understanding of physical, psychological and social factors that contribute to aging, as patients shared their stories. We close with thoughts regarding future steps to promote healthy lifestyle in context of successful aging strategies.
Introduction: Birt-Hogg-Dubé syndrome (BHDS) is a rare autosomal dominant disorder that causes mutations in the Folliculin gene, which predisposes individuals to pulmonary cysts, spontaneous pneumothorax, renal neoplasms, and numerous cutaneous manifestations. The incidence of BHDS is not well understood, as current publications rely on families with known mutations, however it is suspected to be underdiagnosed. In this case we present a young male with recurrent spontaneous pneumothorax who was subsequently found to have BHDS.

Case Report: A 30-year old African American male with past medical history of a spontaneous right-sided pneumothorax three years prior who presented with shortness of breath and right sided chest pain while running. A chest radiograph subsequently confirmed a right lower lobe pneumothorax and soon after a twenty-eight French chest tube was placed to suction. On further review he reported a history of spontaneous right-sided pneumothorax three years prior that was treated with right apical lung bleb wedge resection along with pleurodesis. The following year a 2 centimeter (cm) mucocele was resected from the right lower lobe. Family history was significant for his father and paternal uncle having multiple pneumothoraces. Following removal of his chest tube, he developed a hydropneumothorax in his right basilar lung. His hydropneumothorax increased in size which precipitated a repeat tube thoracostomy. A non-contrast computed tomography (CT) scan was obtained to evaluate for an underlying bullous disease and found multiple pulmonary cysts in both the right and left peripheral lung parenchyma. Given the patient’s family history of spontaneous pneumothorax and the CT evidence of bullous disease, genetic sequencing was done to evaluate for hereditary conditions. He was found to have a novel mutation in the Folliculin (FLCN) gene that has not been documented in prior literature. This confirmed the diagnosis of Birt-Hogg-Dubé syndrome.

Discussion: Birt-Hogg-Dubé syndrome is an autosomal dominant disorder causing a mutation in the FLCN gene which is hypothesized to act as a tumor suppressor protein. The three major features of BHDS are cutaneous manifestations, pulmonary cysts or spontaneous pneumothorax, and renal tumors. Studies have found that between 70-80% of affected patients have multiple pulmonary cysts. Roughly 30% of patients that are subsequently diagnosed with BHDS present with single or multiple spontaneous pneumothoraces. In this case, the patient was ultimately diagnosed after recurrent pneumothorax. He was found to have a new mutation in the folliculin gene that has not been documented in prior literature. His initial presentation should have prompted further investigation into genetic conditions that predispose patients to spontaneous pneumothoraces, such as BHDS.
INTRODUCTION: An atrioesophageal fistula is a connection between the esophagus and the left atrium that can arise in the days to months after atrial fibrillation catheter ablation. It is an extremely dangerous condition where prompt surgical intervention is the only known treatment.

CASE DESCRIPTION: A 62-year-old male with a history of metastatic gastrointestinal stromal tumor (GIST) and atrial fibrillation presented for chest heaviness, nausea, weakness, and right leg tingling. The patient had a left atrial catheter ablation 1 month and 8 days prior to admission. On admission, the patient had a temperature of 100.0°F, a pulse of 121, and an elevated lactate. Shortly after admission, the patient developed right arm numbness and weakness, concerning for a new stroke. A brain MRI was performed which showed multiple lesions throughout the brain. A CT of the chest, abdomen and pelvis showed moderate bilateral pleural effusions, bilateral kidney lesions and liver lesions, which were suspicious for embolic infarcts. Blood cultures grew Strep anginosus and Strep salivarius, organisms usually from the oral cavity. A transthoracic echocardiogram did not note any valvular abnormalities, but during the procedure, a mobile structure was seen in the left atrium that travelled across the mitral valve, and disappeared. After discussion with Cardiology, consideration was given for an atrioesophageal fistula. The fistula could not be visualized on chest CT, so a decision was made to go forward with an esophagogastroduodenoscopy. A 3 mm fistulous opening was seen at the mid-esophagus. The patient continued to have new neurologic symptoms and a follow-up MRI of the brain showed new lesions throughout the brain. An effort to close the fistula on the esophageal side with clipping through an EGD was attempted but was unsuccessful. 8 days after admission, Cardiothoracic Surgery performed an operation to repair the left atrial fistula. After the operation, the patient was minimally responsive and a repeat brain MRI showed multiple new lesions, including a large lesion in the pons. The patient, ultimately, could not be weaned off the ventilator. After discussion with his next of kin, he was terminally extubated and expired shortly thereafter.

DISCUSSION: This case highlights a rare, but dangerous complication left atrial catheter ablation. Our patient expired 1.5 months after the ablation. He had several encounters with the healthcare system, before this complication was ultimately discovered. It is important for all frontline providers to be aware of this condition and intervene promptly for these patients to have any chance for survival.
**DIFFUSE LARGE B CELL LYMPHOMA – MULTIFOCAL EXTRANODAL DISEASE**

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**Introduction:** Diffuse large B cell lymphoma (DLBCL) is a common subtype of non-Hodgkin lymphomas (NHL), making up approximately 30% of cases. Germinal center B cell (GCB) subtype accounts for roughly 40% of DLBCL, has a more favorable prognosis, and is less likely to have extranodal disease compared to non-GCB DLBCL. While extranodal involvement itself is not unique, multiple sites of involvement are rare. We present a unique case of multifocal extranodal DLBCL that presented with hip pain.

**Clinical Vignette:** Patient is a 26 year old active duty man with no significant medical comorbidities. He initially presented to his primary care manager for dull, constant pain in his right hip and groin. There was no antecedent trauma, and he was managed conservatively. Over the subsequent months, his pain progressed to the point of limiting his mobility and interfering with sleep quality. A 7 lb. weight loss was noted. An MRI of the right hip was significant for a marrow infiltrating lesion of the proximal femur with a large soft tissue mass (18.5 X 12.8 X 11.9 cm) with intra-pelvic extension. A PET-CT demonstrated multiple hypermetabolic lesions including a pelvic mass with involvement of right proximal femur, cervical lymphadenopathy, diffuse thyroid uptake, lung nodules, pancreatic masses, stomach, multiple nodules in the kidneys bilaterally, and scattered osseous disease. An MRI brain was negative and CSF obtained via lumbar puncture was negative for malignant cells. A core biopsy of the right hip demonstrated DLBCL, GCB subtype by CD10 positivity, clinical stage IV. He was started on treatment with dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab. His CNS international prognostic index calculated at 5 (scores 4-6 indicate high risk disease) and will receive high dose methotrexate consolidation for prophylaxis.

**Discussion:** This patient has DLBCL with GCB subtype by immunophenotype, which tends to have a better prognosis and is less likely associated with extranodal disease. In one retrospective cohort study of 443 patients, only 6% had involvement of 4 or more extranodal sites. Our patient had multifocal extranodal with involvement of 6 different sites. Increasing sites of extranodal involvement is associated with worse progression free survival and overall survival, and increases risk for CNS relapse. Clinically, patients with CNS relapse have poor outcomes, which is why appropriate risk stratification is important to determine if CNS prophylaxis is indicated.
A CASE OF ACUTE-ON-CHRONIC LIVER FAILURE IN ERYTHROPOIETIC PROTOPORPHYRIA

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Erythropoietic protoporphyria (EPP) is an acute non-blistering cutaneous porphyria, characterized by germline mutations in ferrochelatase. The resulting deficiency impedes the last step of heme biosynthesis leading to accumulation of protoporphyrin IX in the epithelium, erythrocytes, and hepatocytes. The interaction of ultraviolet light and porphyrin leads to free radical production and causes the photosensitivity classic to the cutaneous porphyrias. Accumulation of porphyrin in the liver can causes a rare but potentially severe hepatopathy. A 56 year-old man with a history of EPP since childhood presented with three days of abdominal pain following prolonged sun exposure. Physical exam was remarkable for scleral icterus. Alanine-aminotransferase was found to be elevated to more than 10 times normal, aspartate-aminotransferase more than 20 times normal, and both Total and Direct Bilirubin to more than 10 times normal. Liver ultrasound was consistent with cirrhosis. Common causes of cirrhosis were ruled out including viral and autoimmune hepatitis, acetaminophen toxicity, alpha-1 antitrypsin deficiency, Wilson disease and hemochromatosis. The patient denied alcohol use or ingestion of known hepatotoxic substances. MRCP was negative for biliary obstruction. MELD score on admission was 21.

Liver biopsy revealed cirrhosis, marked cholestasis and red birefringent crystalline material in a Maltese cross formation. Erythrocyte and Plasma porphyrin levels were found to be elevated, and genetic testing confirmed EPP.

The patient was treated with ursodiol, cholestyramine and vitamin E. ON expert consultation, the patient underwent plasmapheresis and received hematin with an ensuing drop in porphyrin levels and Aminotransferase levels. However, total and direct bilirubin levels continued to rise. The patient’s hospital course was complicated by ischemic colitis with intestinal pseudo-obstruction. Oral medications were held, intravenous antibiotics were started. He then developed hypoxia and worsening abdominal distension requiring oxygen supplementation. Paracentesis was performed for a new complex ascites. He developed acute kidney injury with hyperkalemia necessitating continuous renal replacement therapy. Serum porphyrin levels and liver function tests rose and he developed a coagulopathy. MELD rose from 21 to 33 over the course of 3 days. While awaiting transplant he developed hematemesis from ruptured esophageal varices, resulting in sepsis and mixed shock, necessitating intubation and transfer to the ICU. Despite aggressive antibiotic therapy and hemodynamic support, on hospital day 30, he suffered an asystole cardiac arrest and expired.

This case illustrates the rapidity in which acute liver failure can develop from EPP related hepatopathy. There are unfortunately few options for early intervention in EPP. Close serial monitoring of liver function may help identify patients who are at high risk for hepatic failure. These patients may benefit from liver transplantation at a lower threshold.
HICCUM’S DICCTUM: A CASE OF COMBINED HEPATOCELLULAR-CHOLANGIOCARCINOMA

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Combined Hepatocellular-Cholangiocarcinoma (cHCC-CC) is a rare and devastating form of primary hepatic malignancy. As common practice allows for the diagnosis of the most common type of hepatic malignancy (Hepatocellular Carcinoma (HCC)) to be made by imaging without histologic confirmation previous estimates of cHCC-CC incidence may be inaccurately low. This is of concern as cHCC-CC behaves more aggressively than either HCC or Cholangiocarcinoma (CC) alone and therefore requires a different therapeutic approach [1].

A 62-year-old man with limited healthcare exposure reported to the emergency room due to one week of abdominal bloating, distention, and anorexia. CTA of the pelvis showed a cirrhotic liver and multiple hepatic masses the largest of which measured 5 cm in diameter. MRI with liver protocol revealed a heterogeneous increase in T2 signal predominately in the right hepatic lobe compatible with infiltrative HCC. Labs were notable for an elevated AST (446 IU/L on admission; peak of 1713 IU/L), ALT (199 IU/L; 673 IU/L), Total Bilirubin (5.3 mg/dL; 12.6 mg/dL), CA 19-9 (209 U/mL), and AFP (25.3 ng/mL). The patient was found to be Hepatitis C positive with a quantitative HCV RNA of 1,200,000 IU/mL. Interestingly there was also laboratory evidence of spontaneous tumor lysis syndrome with an elevated LDH (peak of >2500 IU/L), Potassium (peak of 6.7 mg/dL), Uric Acid (peak of 12.3 mg/dL) [2]. Liver surgery felt the patient was not a candidate for resection due to large tumor size and poor underlying liver function. Patient was also deemed not to be a candidate for transplant as he did not meet the Milan or UCSF criteria. Medical oncology requested that a liver biopsy be performed to confirm radiographic findings (a Li-Rads classification was not assigned in the report). Liver core needle biopsy subsequently showed evidence of cHCC-CC with positive Hepar1, Glypica, Cytokeratin 7/20, Villin, and CA 19-9. With progressing liver and renal failure the patient was not deemed a good candidate for aggressive chemotherapy. The patient subsequently elected to be placed on comfort care and expired on day 15 of hospitalization.

This case illustrates three salient teaching points. First, it underlines the relatively aggressive nature of combined hepatocellular-cholangiocarcinoma when compared to its individual counterparts. Second, it challenges whether laboratory evidence of tumor lysis in primary hepatic malignancies can be solely attributed to a side effect of immunotherapy or chemotherapy [2], [3], [4], [5]. Finally, this case highlights the importance of using multiple points of information before deciding to forgo biopsy in a presumed case of HCC [6].
Introduction: Brucellosis is a zoonotic infection that may compromise a variety of organ systems including the musculoskeletal, cardiovascular, and nervous system. While endemic to a number of developing countries, cases in the U.S. are rare. Neurobrucellosis is especially infrequent, with only 5-7% of cases affected. Owing to its rarity, protean clinical manifestations, and difficulties with isolating the organism in laboratory specimens, brucellosis is often overlooked or misdiagnosed, especially in non-endemic areas.

Case Presentation: A 60-year old male smoker who owns a farm in Hilo, HI presented with an acute onset of slowed mentation and aphasia. This was on a background of an insidious onset of unexplained progressive low back pain, bilateral hearing loss, malaise, anorexia, weight loss, intermittent headaches, and gait instability with dizziness over several months. Initial work up with a head CTA showed a focally elevated perfusion in the cortex, which was further demonstrated as subarachnoid space disease with leptomeningeal enhancement on follow-up brain MRI. CSF analysis demonstrated markedly elevated WBC (lymphocyte predominant), low glucose, high protein, and a negative gram stain. Findings were concerning for leptomeningeal carcinomatosis or meningitis, and thus patient was started on empiric acyclovir, ceftriaxone, and vancomycin and an exhaustive search for a primary malignancy was undertaken. All initial cultures and PCR evaluations for Tuberculosis, HSV, HIV, and fungal disease were negative, and no malignant process was identified. However, steady clinical improvement was observed in both acute and chronic symptoms on the initial antibiotic regimen, prompting further consideration for an infectious etiology. Additional history obtained by the Infectious Disease consultant revealed a history of slaughtering and consuming raw goat meat. Based on the exposure and patient’s clinical syndrome, neurobrucellosis was suspected. Antibiotics were narrowed to triple-therapy ceftriaxone, doxycycline, and rifampin and the patient thereafter showed consistent improvement of his symptoms. Brucellosis specific serology was ultimately positive for IgG with an undetectable IgM. Isolation of Brucella in CSF and blood specimens were unsuccessful. A presumptive diagnosis of chronic brucellosis complicated by neurobrucellosis was made, and patient was discharged with plans to continue antibiotics until CSF normalization.

Conclusion: This case illustrates the diagnostic challenge of Brucellosis and the value of a complete history. Recognition of potential exposure is key in the diagnostic process as the clinical manifestations are often non-specific. Furthermore, neurobrucellosis should be considered in patients presenting with chronic aseptic meningitis or unexplained neurological symptoms—particularly progressive sensorineural hearing loss—even in the absence of fever. This case also reinforces the importance of keeping a wide differential in mind to prevent any delays in diagnosis.
Poster #25

DESCRIPTIVE STUDY OF HOSPITAL ONSET C. DIFFICILE INFECTION AT THE QUEEN’S MEDICAL CENTER: QUALITY IMPROVEMENT PROJECT

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Introduction: As a part of Value-Based Purchasing program measures, it is critical to lower Clostridium difficile infection (CDI) rates. The 2018 Infectious Disease Society of America guideline for CDI defined healthcare facility-onset (HO) CDI as laboratory-identified events collected more than 3-days after admission to the facility. To implement a strategy to lower CDI rates, there is a need to better understand the current practice trends for CDI. Therefore, we particularly looked at HO-CDI at The QMC to understand the current practice trends.

Methods: We collaborated with the infection control department at The QMC to obtain publicly available rates of HO-CDI between fiscal year (FY) 2017-2018. We obtained testing and HO-CDI rates and compared them to The Centers for Disease Control and Prevention (CDC) national data. We analyzed HO-CDI data for distribution of age, ethnicity, admission source, sex, and diagnostic methods. We also obtained data for laxative use among patients who tested positive for HO-CDI. We also calculated the charges of CDI testing and personal protective equipment to better delineate costs.

Results: For FY 2017-2018, testing rates at The QMC were 10.5/1000 patient-days and 10.9, respectively in comparison to CDC data of 16.3. For HO-CDI rate, 0.57/1000 patient-days and 0.51, respectively, compared to 0.84 for CDC data. 164 patients were identified as having HO-CDI between FY 2017-2018. 55% of the samples were male. Age had a normal distribution with patients in their 70s having the highest HO-CDI rate. Ethnic distribution showed 29% Caucasian, 22% East Asian, 20% Part-Hawaiian, 15% Southeast Asian, and 11% Polynesian. 78% of patients were admitted from home and 13% came from long term care facilities. Homeless patients accounted for only 7%. 58% of tests reflexed to PCR, 36% showed both glutamate dehydrogenase and toxin positive, and 5% had gastrointestinal multiplex PCR positive. 46 patients (28.05%) were using one or more laxatives within 24 hours and 62 patients (37.8%) had laxative use within 48 hours. Polyethylene glycol (12.80%), Sennosides/docusate sodium (12.20%) and docusate sodium (11.59%) were the three most common laxative utilized. Charges associated with CDI testing were: multiplex PCR $171.54, GDH/Toxin $18.45 and C. difficile PCR $42.58. One box of gloves (250 each) and isolation gowns (15 each) were $9.56 and $4.10, respectively.

Conclusion: Although testing and HO-CDI rates were lower than CDC data at QMC, we identified a large number of patients prescribed concomitant laxatives when CDI testing was performed. There is a need to implement institutional CDI testing guidelines among patients using laxatives.
GEOGRAPHIC VARIATION IN INPATIENT MORTALITY RELATED TO GASTROINTESTINAL BLEEDING

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Background: Acute gastrointestinal bleeding (GIB) in adults remains a significant cause of inpatient morbidity and mortality in the U.S. Little is known, however, about what factors may be associated with GIB outcomes, including geographic variation. We designed a descriptive study of inpatient mortality related to GIB in Hawai‘i as compared with other states.

Methods: In this preliminary study, we examined inpatient discharges for GIB using publicly available data from the National Inpatient Sample/Healthcare Cost and Utilization Project. International Classification of Diseases (9th revision) codes 578.0, 578.1, and 578.9 were used to identify the principal diagnosis of GIB for hospital discharges in 2014 (the last year for which solely ICD-9 codes were reported). We obtained state-level information on number of discharges, mean age, sex, length of stay (LOS), and inpatient mortality during GIB hospitalizations. We report discharge rates standardized to the 100,000 general population using U.S. census data from 2014. We used multiple linear regressions to estimate the effect of age, sex, LOS, and state discharge rate on mortality during hospitalizations for GIB. We report R-squared as a measure of the variance in mortality across states which may be explained by geography and the covariates in the regressions.

Results: Among 36 states for which state aggregate data were available from the NIS, the discharge rate for GIB had mean±Standard Deviation of 68.3±15.2 per 100,000 population: highest in West Virginia (105.2), while Hawai‘i had the 6th lowest discharge rate (55.9). Mean age for GIB hospitalizations were summarized by 68.5±2.4 years across states, highest in Vermont (73.3) and third highest in Hawai‘i (71.4). LOS related to GIB discharges were summarized by 3.8±0.5 days, highest in New York (4.9) and 4.1 in Hawai‘i. Women comprised the highest proportion of GIB hospitalizations in Nebraska (52.8%), as compared with Hawai‘i (46.5%). Unadjusted inpatient mortality during GIB hospitalization were summarized by 3.11±0.70%, second highest in Hawai‘i (4.55%), after Vermont (5.25%). Only adjusting for age (adjusted R-squared, 5.7%), Hawai‘i had the third highest adjusted mortality rate (3.35%, vs. 5.45% in Iowa vs. 3.51% in Vermont). Adjusting for age, sex and LOS (adjusted R-square d, 11.7%), Hawai‘i had the second highest adjusted mortality rate (3.71%, vs. 3.96% in Vermont).

Conclusion: In 2014, inpatient mortality during GIB hospitalizations was higher in Hawai‘i than all other states examined, after adjusting for age, sex, LOS and discharge rate. Further studies are needed to confirm these findings and to determine how other factors (including ethnicity) may be associated with the observed mortality differences.
Introduction: Sinus tachycardia and atrial fibrillation are common tachyarrhythmia seen in hyperthyroidism and thyroid storm. Ventricular tachycardia (VT) is seen in patients with underlying heart failure or structural heart disease. In this case a young, previously healthy man presented with recurrent episodes of sustained ventricular tachycardia in the setting of mild biochemical hyperthyroidism and impending thyroid storm.

Case Presentation: A 19-year-old Korean sailor with an unspecified thyroid disorder initially presented to his medical clinic with palpitations and lightheadedness. An electrocardiogram (ECG) was obtained and showed sustained monomorphic ventricular tachycardia (VT) with morphology consistent with an origin within the right ventricular outflow tract. He was given labetalol, which terminated the rhythm. Labs were drawn and were significant for undetectable thyroid stimulating hormone (TSH) with elevated free T3 and T4. He was started on treatment for thyroid storm with propylthiouracil, atenolol, and cholestyramine. A cardiology consult was obtained to evaluate for structural heart disease or ischemia as the precipitant of his sustained ventricular tachycardia. Cardiac imaging studies were ordered to include computed tomographic coronary angiography, an echocardiogram, and subsequent cardiac MRI. These revealed evidence of fibrofatty replacement of the right ventricle consistent with the diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC). He had no further events of sustained VT during his hospitalization and he was discharged with a Life Vest for his travel home.

Discussion: Excessive thyroid hormone can cause a propensity towards cardiac arrhythmias by upregulating several cardiac proteins, including a number of ion channels of the myocardial membrane. Collectively, these changes shorten the duration of the action potential, accelerate depolarization, and shorten the refractory period, making the myocardium susceptible to reentrant tachyarrhythmias. In structurally normal hearts, this can result in sinus tachycardia or atrial fibrillation in up to 28% of patients with hyperthyroidism. Ventricular arrhythmias in the setting of thyrotoxicosis have been uncommonly documented in patients with underlying structural heart disease. Our patient did not initially seem to have any of these predisposing conditions and his degree of hyperthyroidism was inconsistent with clinical presentation, prompted cardiac imaging. His myocardial structure unexpectedly revealed changes consistent with ARVC, which were only manifested in the excitatory milieu of a chronic hyperthyroid state.

Conclusion: We present the case of a patient with a frequently deadly, genetically acquired structural heart disease that was unmasked by thyrotoxicosis and the resultant arrhythmogenic state. Since his underlying disease was uncovered serendipitously, our patient was able to receive appropriate treatment aimed at preventing sudden cardiac death in ARVC.
FACTORS THAT AFFECT PATIENT FITNESS & BODY COMPOSITION DURING HEMATOLOGIC STEM CELL TRANSPLANTATION FOR HEMATOLOGIC MALIGNANCIES

Chelsea Yin, Lindsey J. Anderson, PhD, Stephanie Crabtree, RD, Dorota Migula, RN, Kelsey Geiss, Solomon Graf, MD, Thomas Chauncey, MD, PhD, Jose M. Garcia, MD, PhD
University of Hawai’i John A. Burns School of Medicine, Honolulu, Hawai’i

Hematopoietic stem cell transplantation (HCT) is a potentially curative treatment for hematologic malignancies but is associated with significant side effects, including functional impairment & decreased quality of life (QOL). Poor characterization of HCT-induced functional impairment & prognostic markers for recovery are a barrier to identifying patients at risk & developing new preventive or treatment strategies. This pilot study aims to characterize factors that contribute to these side effects during HCT. Twenty-one patients (autologous = 15, allogeneic = 6) seeking treatment for hematologic malignancy at the Puget Sound Veterans Affairs Healthcare System Bone Marrow Transplant Unit completed measurements of fitness, body composition, sex hormones & inflammation before HCT & 30±10 days after HCT. Blood tests included bioavailable testosterone, estradiol, estrone, IL-6 & TNF. Resting energy expenditure (REE) was assessed by indirect calorimetry, body composition by dual-energy x-ray absorptiometry & functional performance by handgrip strength (HGS), stair climbing power (SCP), 6-minute walk test (6MWT), 1-repetition maximum (1RM) muscle strength, chair stand test (CST) & peak oxygen consumption (peak VO2). Previously-validated questionnaires were used to assess QOL & functional status. Statistical methods included non-parametric paired t-tests. Both groups showed significant decreases in 6MWT (autologous, p=0.009, allogeneic, p=0.046) & patient-reported vitality (autologous, p=0.03, allogeneic, p=0.04) at follow-up. The autologous group also showed significant decreases in peak VO2, HGS, SCP, CST, lower body 1RM, fat mass, lean mass, REE, estrone, erectile function & sexual desire (p≤0.05). These parameters were unchanged after allogenic transplant. Bioavailable testosterone, estradiol, IL-6 & TNF were unchanged in both groups. The autologous group reported significantly increased nausea, & diminished social/family well-being (p≤0.03), with a trend for increased fatigue (p=0.053). Recruitment & long-term follow up are ongoing. HCT is associated with a significant decline in fitness & muscle function & increased burden in patient reported outcomes.
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