

Sponsored by the 8 Permanente Medical Groups

Mission: *The Permanente Journal* advances knowledge in scientific research, clinical medicine, and innovative health care delivery.

Circulation: 2 million page views of *TPJ* articles in PubMed from a broad international readership



Fall Foliage
photograph
Monica Leigh

In the woods near my house, where I walk my dog on a regular basis, this rustic stairway emerges. It transports one from a narrow foot path to an open field. As COVID-19 has kept us all closer to home, the woods have become a regular sanctuary, a place where I and my dog can roam freely, forgetting about the worries that weigh me down at home. On this sunny day—November 7, 2020—things seemed particularly hopeful. There was talk of a vaccine, and the idea of a new beginning for 2021 emerged. I like to think of this image as a visual reminder that we will find a way out of the depths of disease and into a hopeful future where we can visit and hug our loved ones, travel and discover new places, and meet new friends without fear of infection.

Monica Leigh is a senior managing editor for KWF Editorial and the managing editor for *The Permanente Journal*. When she isn't fostering scientific discovery through scholarly publishing, she photographs families in the Baltimore area and enjoys spending time in nature with her family and their dog.



EDITORIAL & PUBLISHING OFFICE

The Permanente Journal
c/o Laura Fegraus
1 Kaiser Plaza, 27th Floor
Oakland, CA 94612
Email: permanente.journal@kwfco.com

INSTRUCTIONS FOR SUBMISSION

Instructions for Authors are available along with a link to our manuscript submission center at www.thepermanentejournal.org/authors.html

PERMISSIONS AND REPRINTS

Reprint Permission Form available at:
www.thepermanentejournal.org/about-us/5818-reprint-permissions.html

The Editorial Staff have disclosed that they have no personal, professional, or financial involvement in any of the manuscripts they might judge. Should a conflict arise in the future, the Editorial Staff have agreed to recuse themselves regarding any specific manuscripts. The Editorial Staff also will not use the information attained through working with manuscripts for private gain.

TABLE OF CONTENTS

ORIGINAL RESEARCH & CONTRIBUTIONS

1 High Remission Rate with Infliximab and Plant-Based Diet as First-Line (IPF) Therapy for Severe Ulcerative Colitis: Single-Group Trial. Mitsuro Chiba, MD, PhD; Tsuyotoshi Tsuji, MD, PhD; Kunio Nakane, MD, PhD; Satoko Tsuda, MD; Hajime Ishii, MD, PhD; Hideo Ohno, MD; Yu Obara, MD; Masafumi Komatsu, MD, PhD; Haruhiko Tozawa, MD

About one-third of patients with severe ulcerative colitis (UC) do not respond to corticosteroid therapy and receive rescue therapy with infliximab or cyclosporine. Up to 20% of such patients fail to respond to rescue therapy and undergo colectomy. Patients with severe UC defined by the Truelove and Witts criteria were admitted and given standard induction therapy with infliximab (5.0-7.5 mg/kg) at 0, 2, and 6 weeks. Additionally, they received a PBD. The primary endpoint was remission or colectomy in the induction phase and 1 year after discharge. Secondary endpoints were changes in inflammatory markers in the induction phase and the PBD score at baseline follow-up. A higher PBD score indicates greater adherence to a PBD.

11 Refill Reminder Preference and Inhaled Corticosteroid Adherence Among Patients with Asthma. Marsha A Raebel, PharmD; Susan M Shetterly, MS; Glenn K Goodrich, MS; Courtney B Anderson, MPH; Bruce G Bender, PhD; Nicole M Wagner, PhD

Refill reminders can help patients improve adherence to inhaled corticosteroid (ICS) therapy. However, little is known about patient preferences for reminder type or whether patients who express a preference differ from patients who do not. Among patients who expressed a preference, text reminders were preferred. Patients who expressed a preference had higher baseline adherence. Further research is needed to determine whether expressing a preference for a refill reminder type is itself associated with adherence. Given that offering the opportunity to choose a reminder type only engaged a subset of patients, further work is needed to understand how best to leverage technology-enabled communication outreach to help patients optimize adherence.

19 Clinical Implications of the Association of Race With Body Satisfaction and Perceived Control Over Eating in Women Initiating a Behavioral Obesity Treatment. James J Annesi, PhD, FAAHB, FTOS, FAPA; Ping H Johnson, PhD

An improved understanding of the implications of race on body satisfaction might optimize the weight loss process and quality of life in women with obesity. The findings of this study increased understanding of body satisfaction in women with obesity and have implications for addressing psychosocial factors within weight loss treatments across racial and at-risk groups.

24 Physicians' Views on a Wellbeing Course Gifted to Them: A Qualitative Study. Patricia Lynn Dobkin; Camila Velez

Given concerns about staff burnout and distress, the Chief of the Department of Medicine sponsored the Physician Wellbeing program making it cost-free for doctors at a large academic medical setting. Ninety doctors registered within the one-year pilot project time frame. Following a Mind-Body Medicine online and Mindful Medical Practice workshop a qualitative study was conducted to identify physicians' views about the initiative. Physicians who agreed to take part following the workshops were the participants in the study. Physicians supported the integration of wellness programs into medical settings where stress is an inherent aspect of the work environment. They were grateful for the "gift" of being valued and supported by the administration.

32 Evaluation of Dipeptidyl Peptidase-4 Inhibitors versus Thiazolidinediones or Insulin in Patients with Type 2 Diabetes Uncontrolled with Metformin and a Sulfonylurea in a Real-World Setting. Natalie Aboubechra, PharmD, BCPS; Vittoria Marie Ledesma, PharmD, BCPS; Fang Niu, MS; Susan M Lee, PharmD, BCPS; Yesha A Patel, PharmD, BCPS; Mirta Millares, PharmD, FCSHP, FASHP; Rita L Hui, PharmD, MS

To compare effectiveness and safety of dipeptidyl peptidase-4 inhibitors (DPP4i) to thiazolidinedione (TZD) or insulin as third add-on agent to metformin plus sulfonylurea in an integrated healthcare setting. This retrospective database cohort study included adults with T2D not at goal hemoglobin A1c (A1c) who initiated a DPP4i, TZD, or insulin as third add-on agents to metformin plus sulfonylurea from January 2006 to June 2016. Primary outcomes were the proportion of patients who achieved goal A1c after starting the third add-on agent and change in A1c. Subgroup analysis was performed in patients with baseline A1c > 9%.

40 Knowledge, Attitudes, and Perceptions About Medicolegal Education: A Survey of OB/GYN Residents. Shilpa Mathew, MD, JD; Navendu Samant, PhD; Christie Cooksey, MD, MSCR; Olga Ramm, MD, MS

Medicolegal concerns affect the career decisions of OB/GYN residents; however, their exposure to medicolegal education during residency training is virtually unknown. Exposure to medicolegal topics during OB/GYN residency training is very limited and unstructured. This study shows that residents desire a more formalized medicolegal curriculum during postgraduate training and that implementation may have several benefits.

- 47 Characteristics Associated with Participation in ENGAGED 2 – A Web-based Breast Cancer Risk Communication and Decision Support Trial.** Karen J Wernli, PhD; Erin A Bowles, MPH; Sarah Knerr, PhD; Kathleen A Leppig, MD; Kelly Ehrlich, MS; Hongyuan Gao, MS; Marc D Schwartz, PhD; Suzanne C O'Neill, PhD

We evaluated demographic and clinical characteristics associated with participation in a clinical trial testing the efficacy of an online tool to support breast cancer risk communication and decision support for risk mitigation to determine the generalizability of trial results. Use of plain language and potential access to a website providing personal breast cancer risk information and education were insufficient in achieving representative participation in a breast cancer prevention trial. Additional methods of targeting and tailoring, potentially facilitated by clinical and community outreach, are needed to facilitate equitable engagement for all women.

- 55 Patients' Experiences with Refilling their HIV Medicines: Facilitators and Barriers to On-Time Refills.** Syundai R Johnson, MPH; Thomas P Giordano, MD, MPH; Christine Markham, PhD; Sarah Njue-Marendes, MPH; Bich N Dang, MD

Adherence to antiretroviral therapy (ART) is particularly important for patients with human immunodeficiency virus (HIV). Prior research on ART adherence has focused primarily on behavioral interventions targeting patients and providers. No study has focused on the pharmacy refill experience as a potential target for improving adherence to HIV medicines. Informed by patients' experiences, this study aimed to: 1) assess patients' experiences with refilling their HIV medicines, and 2) explore facilitators and barriers to refilling medicines on time.

- 64 Demographic, Clinical, and Prescribing Characteristics Associated with Future Opioid Use in an Opioid-Naive Population in an Integrated Health System.** David M Mosen, PhD, MPH; A Gabriela Rosales, MS; Rajasekhara Mummadi, MD, MPH; Weiming Hu, MS; Neon Brooks, PhD

Health systems and prescribers need additional tools to reduce the risk of opioid dependence, abuse, and overdose. Identifying opioid naive individuals who are at risk of opioid dependence could allow for the development of needed interventions. By identifying population characteristics associated with continued opioid use following a first prescription, our data pave the way for quality improvement interventions that target individuals who are at higher risk of opioid dependence.

- 70 Evaluation of a Motivation-Based Intervention to Reduce Health Risk Behaviors among Black Primary Care Patients with Adverse Childhood Experiences.** Ellen Goldstein, PhD; James Topitzes, PhD; Susan Flowers Benton, PhD; Kathleen P Sarino, BS

Considerable evidence suggests that greater attention should be paid to the impact of trauma among low-income, racial/ethnic minority patients living in urban communities. The goal of this paper is to evaluate a two-session, motivational intervention designed to motivate a change in health risk behaviors among low-income, self-identified Black/African American patients with adverse childhood experiences (ACEs).

- 79 The Potential Protective Effect of Hope on Students' Experience of Perceived Stress and Burnout during Medical School.** Ashten R Duncan, MPH; Chan M Hellman, PhD

A major problem facing today's physicians and medical students is burnout. Burnout has been described as a product of chronic stress and a lack of protective psychological factors like hope by Christina Maslach and fellow researchers. The purpose of this study was to explore the relationships between hope, stress, and burnout among medical students. Hope may play a significant protective role in the stress-burnout relationship in the context of medical students: higher levels of hope are associated with lower levels of stress and burnout. Our study supports the idea of using hope-based interventions in medical student populations and investing more resources into this area of research.

- 86 Routine Screening for Sepsis in an Obstetric Population: Evaluation of an Improvement Project.** Holly A Champagne, DNP, RN; Matthew J Garabedian, MD

Our objectives were to calculate the timeliness of treatment following implementation of routine sepsis screening in an inpatient obstetric population using obstetric-adjusted systemic inflammatory response syndrome (SIRS) criteria, evaluate the performance of obstetric-specific screening criteria in the identification of sepsis, and to better characterize the frequency of end-organ dysfunction associated with those who met the definition of sepsis. Pregnant and newly-delivered women benefitted from implementation of routine sepsis screening, as this resulted in timely initiation of treatment.

- 96 A Reconceptualization of the Negative Self-Stereotyping of the Patient-Partner to the Introduction of the Patient Perspective Consultant.** Richard B Hovey, MA, PhD.; Veeresh Pavate, MEd (PhD student); Marie Vigouroux, BA (M.Sc. Student); Kristina Amja, BSc (M.Sc. Student)

The label of patient-partner (PP) is widely used when referring to a person living with a specific health condition who participates in research teams or consults on clinical practice guidelines. However, being a patient-partner says nothing about one's potential role outside a biomedical context. Labelling a person as such can be detrimental to their perception of themselves. The intention of this paper is to provide a philosophical conceptual framework to understand the complexities and consequences of labelling people as patients outside of direct healthcare.

- 102 Prevalence and Characteristics of Chronic Cough in Adults Identified by Administrative Data.** Robert S Zeiger, MD, PhD; Fagen Xie, PhD; Michael Schatz, MD, MS; Benjamin D Hong, MS; Jessica P Weaver, MPH; Vishal Bali, MS, PhD; Jonathan Schellhout, PhD; Wansu Chen, MS, PhD

International Classification of Diseases-9/10 codes for chronic cough (CC) do not exist, limiting investigation. This observational study using administrative data identified hierarchically patients aged 18-85 years with CC from 2013-2016. First, a specialist-diagnosed CC group was identified using an internal CC encounter code during an outpatient visit to a pulmonologist, allergist, otolaryngologist, or gastroenterologist. Subsequently, an event-diagnosed CC group was identified based on clinical notes through natural language processing, ICD-9/ICD-10 cough codes, and dispensed antitussives.

- 116 Validation Study of Kaiser Permanente Bedside Dysphagia Screening Tool in Acute Stroke Patients.** Barbara Schumacher Finnegan, MA, RN, CPHQ; Melissa M Meighan, DNP, MS, RN, CNRN, SCR.N, NEA-bc; Noelani C Warren, MSN, RN, SCR.N; Meghan K Hatfield, MPH; Stacey Alexeeff, PhD; Jorge Lipiz, MD; Mai Nguyen-Huynh, MD, MAS

Dysphagia occurs in up to 50% of patients with acute stroke symptoms resulting in increased aspiration pneumonia rates and mortality. The purpose of this study was to validate a health system's dysphagia (swallow) screening tool used since 2007 on all patients with suspected stroke symptoms. Annual rates of aspiration pneumonia for ischemic stroke patients have ranged from 2-3% since 2007. This tool is highly reliable and valid. The dysphagia screening tool requires minimal training and is easily administered in a timely manner.

- 122 Presentation of Rash in a Community-Based Health System.** Jennifer R Dusendang, MPH; Sangeeta Marwaha, MD; Stacey E Alexeeff, PhD; Lisa J Herrinton, PhD

Coordination of care between primary care providers and dermatologists is important to ensure high quality and cost efficiency. In our integrated care setting, we used a retrospective cohort study to assess which patients self-refer to dermatology and which returned for a follow-up visit in dermatology. One percent of patients with a new rash diagnosis self-refer to dermatology in this setting. Patients with a history of a dermatological condition were more likely to self-refer to dermatology and to have a follow-up visit with a dermatologist. Individual dermatologists and primary care providers had little impact on a patient's odds of returning for a follow-up visit.

REVIEW ARTICLES

- 126 A Clinical Approach to Catamenial Epilepsy: A Review.** Samuel Frank; Nichole A Tyson, MD

Catamenial Epilepsy (CE) is a type of epilepsy that is exacerbated by hormonal fluctuations during the menstrual cycle. Approximately 1.7 million women have epilepsy in the United States. CE affects over 40% of women with epilepsy (WWE). There is a paucity of literature addressing this condition from a clinical standpoint and the literature that does exist is limited to the neurological community. This article aims to review the diagnosis and management of CE for the non-neurologist.

- 135 CRISPR/Cas9 for the Clinician: Current uses of gene editing and applications for new therapeutics in oncology.** Julia Boland, MD; Elena Nedelcu, MD

In this review, we will briefly summarize the history and development of CRISPR. Additionally, we will explain CRISPR-Cas systems and CRISPR gene editing tools. Then, we will highlight the development and application of CRISPR technologies for translational and therapeutic purposes in different oncologic tumors. Lastly, we will review novel treatment paradigms using CRISPR in immuno-oncology, including checkpoint inhibitors and chimeric antigen receptor (CAR) T cell therapy.

Contents continued on next page

- 139 Identifying Risk Factors Associated With Postoperative Infection Following Elective Lower-Extremity Total Joint Arthroplasty.** Michelle Lespasio, DNP, JD, NP; Michael Mont, MD; Anthony Guarino, PhD

This review addresses the importance of identifying risk factors associated with postoperative Prosthetic Joint Infection (PJI) following elective lower extremity total joint arthroplasty (TJA). Addressing associated risk factors before surgery is essential to reducing PJI after surgery. Although the literature differentiates risk factors as modifiable or nonmodifiable, we take the position that all risk factors (to some extent) are modifiable prior to elective TJA surgery. Therefore, this review discusses risk factors recognized by the American Academy of Orthopaedic Surgeons (AAOS) that should be carefully considered and assessed by the orthopaedic team in collaboration with the primary care provider (PCP) before proceeding with surgery.

CASE REPORTS

- 149 Management of Spontaneous Liver Hematoma in Ehlers-Danlos Syndrome Type IV: A Case Report.** Brandon Imp, MD; Samuel Mannarino, MD; Anand Narayanan, MD

Liver hematoma is an uncommon feature of Ehlers-Danlos syndrome type IV. The limited literature that exists to guide management does not establish a standard of care. A 26-year-old man presented with acute abdominal pain caused by a large, spontaneous liver hematoma. Invasive prophylactic arterial embolization was done twice, but surgical evacuation was not offered because of concern for poor healing and brittle vasculature, later diagnosed as symptoms of the patient's Ehlers-Danlos syndrome type IV. During hospitalization, the patient died of spontaneous intracerebral and intra-abdominal hemorrhaging.

- 153 Synergistic Effect and Tolerance of Concurrent Radiotherapy and Lenalidomide Use in Relapsing Mantle Cell Lymphoma: A Case Report.** Mariem Bohli, MD; Hager Jaffel, MD; Gaiet El Fida Noubbigh, MD; Sabrina Tbessi, MD; Fehmi Msadek, MD; Lotfi Kochbati, MD

Mantle cell lymphoma is an aggressive disease. Limited treatment options are available for refractory or relapsing presentation. We report the first case, to the best of our knowledge, of concurrent radiotherapy and lenalidomide use in this setting, focusing on its possible synergy and tolerance. This case highlights the role of concomitant lenalidomide treatment and low-dose radiotherapy in patients with relapsing mantle cell lymphoma. Use of this combination treatment has achieved a complete local control with a safe toxicity profile. The case also illustrates the possible lenalidomide-induced radio sensitization.

- 159 Acquired Amegakaryocytic Thrombocytopenia Misdiagnosed as Immune Thrombocytopenia: A Case Report.** Arya Mariam Roy, MD; Manojna Konda, MD; George K Sidarous; Dinesh Atwal, MD; Steven A Schichman, MD, PhD; Anuradha Kunthur, MD

Acquired amegakaryocytic thrombocytopenia (AATP) is a rare bleeding disorder that causes severe thrombocytopenia with preserved hematopoiesis of other cell lineages. Many cases are misdiagnosed and treated as immune thrombocytopenia. We report a case of AATP, in a 50-year-old man, that was treated as immune thrombocytopenia for years with no clinical response. The disorder later was diagnosed as AATP after bone marrow biopsy and was successfully treated with cyclosporine.

- 164 Concurrent Birt-Hogg-Dubé Syndrome and Hereditary Paraganglioma-Pheochromocytoma Syndrome Presenting as Metastatic Renal Cell Carcinoma in a 25-Year-Old Man: A Case Report.** Julia Boland, MD; Darius Shahbazi; Ryan Stevenson, MD; Shahin Shahbazi, MD

Birt-Hogg-Dubé syndrome and hereditary paraganglioma-pheochromocytoma syndrome are rare genetic cancer syndromes that predispose patients to renal neoplasia. We report a case of a 25-year-old man with both Birt-Hogg-Dubé syndrome and hereditary paraganglioma-pheochromocytoma syndrome who presented with painless gross hematuria and was found to have metastatic clear cell renal carcinoma. To our knowledge, this is the first known case report to date documenting a patient with concurrent Birt-Hogg-Dubé and hereditary paraganglioma-pheochromocytoma syndrome. This case demonstrates the exceptionally young presentation of metastatic renal cell carcinoma with this genotype.

- 170 Budd Chiari Syndrome and Intrahepatic Cholangiocarcinoma, An Unusual Combination: Case Report and Review of the Literature.** Anshuman Elhence, MD; Shivanand Gamanagatti, MD; Prasenjit Das, MD; Shalimar, DM

We report a case of intrahepatic cholangiocarcinoma in a patient with primary Budd Chiari syndrome. Hepatocellular carcinoma is known to occur with Budd Chiari syndrome. It was difficult to differentiate from hepatocellular carcinoma in the presence of increased alpha-fetoprotein levels. The contrast imaging showed features of progressive enhancement in the arterial, portal and venous phases. A targeted liver biopsy showed histological features typical for cholangiocarcinoma. Immunostaining for CK 7 and CK 20 were positive, while that for arginase was negative suggesting an intrahepatic cholangiocarcinoma. The patient was planned for inferior vena cava angioplasty followed by resection for intrahepatic cholangiocarcinoma.

- 173 Immunoglobulin A Nephropathy, Celiac Disease, and Immune Complex Pneumonitis: A Rare Case Report of an Immunoglobulin A-Associated Pathologic Trifecta.** A J Mahendran, MD; Nitesh Gupta, DM; Sumita Agrawal, DM; Pranav Ish, DM; Shibdas Chakrabarti, MD

The systemic manifestations of IgA nephropathy with lung involvement include diffuse alveolar haemorrhage (DAH) due to monoclonal IgA disorders, IgA-variant Good pasture's syndrome, and Henoch-Schoenlein purpura (HSP). However, pneumonitis due to IgA immune complex, has rarely been reported as the pulmonary manifestations of IgA nephropathy. Secretory IgA may be acting as an immune complex or proinflammatory agent to provoke the signs and symptoms in this case. Thus, the respiratory process may incite renal disease or vice-versa. Further research is needed to analyse the possibility of such associations.

- 176 Concomitant Large Loculated Pleural and Pericardial Effusions in a Patient with Rheumatoid Arthritis on Methotrexate.** Nakiya Whitfield, PharmD; Anne Krasniak, PharmD; Hien Nguyen, MD

Rheumatoid arthritis is the most common multisystemic autoimmune inflammatory joint disorder that affects nearly 1.3 million adults in the United States. We present the diagnostic challenges of differentiating pleuropulmonary and pericardial complications of rheumatoid arthritis from side effects of therapy (rheumatoid pleural and pericardial effusions versus immune suppression associated side effects and infections). We employ the Naranjo score to facilitate this decision-making process.

- 181 From Dyspepsia to Diagnosis: A Rare Gastric Subepithelial Lesion Definitively Diagnosed via Endoscopic Submucosal Dissection and Immunohistochemistry.** Shreyas Srinivas, MD; Sajjad Syed, MD; Sathima Natarajan, MD; Karl Kwok, MD

Peripheral nerve sheath tumors, known as perineuromas, are typically found on the trunk and extremities. They are less commonly described in the gastrointestinal tract, and extremely rarely are described in the stomach. Since the first case of gastric perineuroma was first described in 2004, there have only been 4 reported cases in the English literature. This case highlights the crucial interdisciplinary multidisciplinary effort between pathologists and GI specialists required to reach this diagnosis, and showcases endoscopic diagnosis using endoscopic dissection which allows for complete lesion resection and complete resolution of the patient's symptoms.

- 185 Possible Precipitation of Acute Coronary Syndrome with Immune Checkpoint Blockade: A Case Report.** Rajeev Masson, MD; Gopi Manthripragada, MD; Raymond Liu, MD; Jahan Tavakoli, MD; Kenny Mok, MD, MPH

Immune checkpoint inhibitors (ICI) have led to improved survival in patients with a number of different tumor types. The ICI agent nivolumab induces anti-tumor immune responses by inhibiting the programmed cell death 1 protein, but side effects include cardiac immune-related adverse events (irAE) such as myocarditis.¹ The association of nivolumab with atherosclerotic disease has been rarely reported. A 62 year old man with metastatic melanoma and recent myocardial infarction (MI) presented with recurrent MI after having undergone several cycles of nivolumab therapy. Repeat cardiac catheterization revealed rapidly progressive in-stent restenosis and diffuse coronary artery disease (CAD) requiring bypass surgery and warranting cessation of nivolumab therapy.

LETTER TO THE EDITOR

- 189 Can Burnout Among Child Abuse Clinicians be Caused by Doubt that They are Doing the Right Thing?.** Niels Lynøe, MD, PhD; Anders Eriksson, MD, PhD

Letter regarding the strong association between burnout among child abuse clinicians and staff working within emergency departments and pediatric palliative care (Passmore et al) including the authors' response.

- 191 ECG Changes in Capecitabine-Induced Takotsubo Cardiomyopathy.** Lovely Chhabra, MD, FACC; Nadine Mohamed, MS

Bhardwaj and colleagues described an interesting Case Report of Takotsubo Cardiomyopathy (TC) in a patient with anal cancer who received chemotherapy with capecitabine, an oral prodrug of 5-fluorouracil (5-FU). Cardiac toxicity is a well reported side-effect of fluoropyrimidine chemotherapies (5-fluorouracil (5-FU) and capecitabine); however, TC is a rare and less commonly known side-effect. TC has been previously reported with the use of 5-FU in some case studies, though other cardiotoxic and systemic side effects of fluoropyrimidine therapies have been well described in large studies.