Greer Memorial Hospital, Greer, SC (part of Greenville Health System)
Orthopaedics at Patewood Ranks Among Nation's Best

Make no bones about it—GHS' Patewood Memorial Hospital has been recognized as a top hospital in orthopaedics by *U.S. News & World Report*!

Patewood Memorial Hospital is #19 in the nation for 2016-17—the only hospital in South Carolina to be ranked in orthopaedics. Patewood also was named High Performing in hip replacement.

In addition, GHS' Greenville Memorial Hospital was named High Performing in three areas: heart failure, colon cancer surgery and chronic obstructive pulmonary disease.

These achievements would not be possible without all members of our healthcare team—doctors, nurses, allied health professionals, support staff and volunteers—combining their joint efforts to deliver high-quality care. Thanks to their skill and dedication, GHS continues its patient-focused mission to *heal compassionately and improve constantly*.

Learn more at [ghs.org/usnews](http://ghs.org/usnews).
The peer-reviewed journal of Greenville Health System

Vision: To transform health care through the publication of relevant, innovative, and multidisciplinary scholarship concerning advancements in clinical, academic, and translational research

Editor-in-Chief: William D. Bolton, MD

Managing Editor: Ally Hale, BA

Associate Editors: A. Michael Devane, MD; Haytham H. Dimashkieh, MD; Jeffrey W. Elder, MD; Timothy P. McHenry, MD; Naveen N. Parti, MD; Jeremy A. Warren, MD

Editorial Board: A. Michael Devane, MD; Haytham H. Dimashkieh, MD; Jeffrey W. Elder, MD; Timothy P. McHenry, MD; Naveen N. Parti, MD; Jeremy A. Warren, MD; Molly Benedum, MD; Susan Bethel, MSN, RN, NE-BC; Parampal Bhullar, MD; Matthew D. Bitner, MD, MEd, FACEP; Eric S. Bour, MD, MBA, FACS, FASMS; John S. Bruch, MD, FACE; Christopher Campen, PharmD, BCOP; Joni Canter, MBA, ATC; Christopher G. Carsten III, MD; Anna L. Cass, PhD, MPH; India Chandler, MD; Catherine M. Chang, MD; F. Tich Changamire, MD, ScD, MBA; Patricia L. Cheek, MD; John D. Cull, MD; Patrick J. Culumovic, MD; James R. Davis, MD; Lauren D. Demosthenes, MD; Kacey Y. Eichelberger, MD; M. Carmela Epright, PhD; J. Alex Ewing, MS; Sarah R. Farris, MD; Lawrence D. Fredendall, PhD; Sagar S. Gandhi, MD; Bruce H. Gray, DO; John B. Hartman II, DMin; Steven B. Holsten Jr, MD, FACS; William W. Hope, MD, FACS; Matthew F. Hudson, PhD; Sandip Jain, MD; Esther M. Johnstone, DNP, MSN, RN, CNOR; Lindsay H. Jones, CRNA; J. William Kelly, MD; Laura H. Leduc, MD; Bruce A. Lessey, MD, PhD; Tina Lindsey, CCP Perfusion; Ervin L. Lowther, MD; Charles G. Marguet, MD; Nancy Markle, RN; Brian P. McKinley, MD, FACS; Paul B. Miller, MD; Ryan Miller, Sr; Ryan Miller, Sr; Embryologist; Benjie B. Mills, MD; S. John Millon, MD; Ivaylo I. Mitsiev, MD; John S. Morris, MD; Phillip Moschella, MD, PhD; Bryce A. Nelson, MD; M. Jason Palmer, MD; Puraj Patel, DO; Nirav T. Patil, MBBS, MPH; Sarah B. Payne-Poff, MD; Larry E. Puls, MD; Krista Ramirez, PharmD, BCPS; Vinayak S. Rohan, MD; Robert A. Saul, MD; Kerry K. Sease, MD; Rhett M. Shirley, MD; Dane E. Smith, MD; John A. Spratt, MD; Antine E. Stenbit, MD, PhD; Michael Stewart, MD; Jeremy Stuart, PhD, MPH; Laurie M. Theriot Roley, MD; Steven D. Trocha, MD; Adam B. Tyson, MD; Diana Vargas Vives, MD; Thomas L. Wheeler, MD; Michael W. Wiederman, PhD; Christopher C. Wright, MD; Yuliya Yurko, MD

Editorial Services: Jeanine Halva-Neubauer, MA; Travis Crump, BS

Produced By: GHS Creative Services

Greenville Health System Proceedings (GHS Proceedings) is a peer-reviewed medical journal that represents the top academic and clinical research activities happening at GHS and throughout the world. GHS Proceedings is published twice a year (spring and fall) and is a primarily online journal constructed of original research, review articles, case reports, editorials, book reviews, and more. GHS Proceedings’ mission is to provide high-quality publications on healthcare innovation and delivery (university.GHS.org/Proceedings).

To receive upcoming issues by email, contact Ally Hale at AHale@ghs.org.
# Table of Contents

## Viewpoint
89 **OPINION** Monoclonal Antibodies, Blood-Brain Barrier and Disability in Multiple Sclerosis: Time for Combination Therapies by Jagannadha Avasarala

92 **TEACHABLE MOMENT** Do I Really Need to Stop Taking Estrogen? by Chelsea W. Fox, Bruce A. Lessey, and Paul B. Miller

94 **VALUE VIGNETTE** Choosing High-Value Care in Suspected Lower Extremity Deep Vein Thrombosis by Moon Won and Steven Connelly

## Special Article
97 Perceptions of and Preferences for a Mobile Health Clinic for Underserved Populations by Melinda Gillispie, Catherine Mobley, Lynette M. Gibson, and Arelis Moore de Peralta

## Original Research

113 Blood Loss and Transfusions After Pericardial Closure Using a Porcine-Derived Extracellular Matrix by Timothy G. Johnson, William W. Hope, Howard F. Marks, and Peter N. Kane

117 Impact of Methicillin-Resistant Staphylococcus aureus (MRSA) Decolonization Protocol on Colonization and Infection Rates in a Level III Neonatal Intensive Care Unit by Myah Griffin, Nirav T. Patil, and Robin N. LaCroix

121 Does Comprehensive Dementia Education Impact Self-Efficacy Among Family Caregivers in the Community? by Xi Pan, Melissa Bailey, Meghan Socko, and Lisa Naylor

126 Insurance Status of Deceased Organ Donors by John D. Cull, Tara L. Spivey, Samuel Kingsley, David A. Ansell, Kimberly Joseph, and Edie Y. Chan

## Case Studies
130 Catastrophic Upper Gastrointestinal Bleed in Roux-en-Y Gastric Bypass Patients From Ulcer Erosion Into the Splenic Artery: Details of Rapid Surgical Management by Andrew J. Jones, Nathaniel Walsh, Aaron Bolduc, Sean Lee, and Brian Lane

133 Dexmedetomidine-Induced Adrenal Crisis in an Infant by Jeremy M. Loberger, Robert S. Seigler, and Michael G. Avant

136 Radiographic Evidence of Diffuse Large B-cell Lymphoma Presenting as Carpal Tunnel Syndrome by Anthony J. Horton and Jeffrey R. Wienke

140 Management of Brujeria, a Culture-Bound Syndrome by Joseph T. Mingoia and Taral R. Sharma

143 Levamisole-Induced Necrosis Syndrome Associated With Cocaine Use by Richard O’Neal and Sheena Henry

---

All statements and opinions expressed in GHS Proceedings are those of the authors and not necessarily those of Greenville Health System, its board, or any of its affiliates.

Guidelines for authors are available at university.ghs.org/proceedings/authors. Completed manuscripts may be submitted online (university.ghs.org/proceedings/submit) or by mail (POSTMASTER: GHS Proceedings, Greenville Health System, 3rd Floor Support Tower, 701 Grove Rd, Greenville, SC 29605)

Copyright © 2016 Greenville Health System. All rights reserved.
Monoclonal Antibodies, Blood-Brain Barrier and Disability in Multiple Sclerosis: Time for Combination Therapies

Jagannadha Avasarala, MD, PhD

From the Department of Medicine, Division of Neurology at Greenville Health System, Greenville, SC (J.A.), and University of South Carolina School of Medicine Greenville, Greenville, SC (J.A.)

Abstract

The treatment of multiple sclerosis (MS) continues to evolve. However, even with the introduction of B-cell-depleting monoclonal antibodies (MAbs), disability progression continues unabated since B-cell therapies with MAbs do not address disease that lurks in the brain. The principal reason MAbs cannot enter the brain is because of their considerable size—limitations in size prevent MAbs from crossing the blood-brain barrier (BBB). To counter this problem, combining drugs that cross the BBB, such as siponimod, cyclophosphamide, or laquinimod with peripherally acting MAbs, could be one option. The concept of combining a small molecule with MAbs is novel from a pharmacologic perspective and follows disease pathophysiology. In this brief report, a fundamentally new idea based on combination therapies designed to address pathology within and outside of the brain/cord is presented. Limitations to such strategies include scant knowledge of the effects of small molecules in suppressing disease in the brain/cord, but it has been 23 years since the first MS drug was approved by the Food and Drug Administration; not a single drug, thus far, halts disability or the inevitable march of disease progression. It is time for scientists and clinicians to consider a different approach in MS therapeutics.

Rapid strides have been made in the treatment of multiple sclerosis (MS) since the Food and Drug Administration (FDA) approved the first drug for use in 1993. Despite these advances, treatment options for worsening disease characterized by accumulating disability on expanded disability status scores (EDSS) or cognitive decline are disappointing and unsuccessful. These outcomes are particularly worrisome for African American (AA) patients who have worse EDSS scores and gait abnormalities at diagnosis, and they likely have more primary progressive MS (PPMS) variants.1

The reason for the relentless progression of disability in relapsing-remitting MS (RRMS) across all racial and ethnic backgrounds that eventually transitions into secondary progressive MS (SPMS) is probably linked to the poor penetration of the blood-brain barrier (BBB) by drugs used in MS therapies in general and monoclonal antibodies (MAbs) in particular. Currently, 3 MAbs have been approved for MS therapy: natalizumab, alemtuzumab, and daclizumab.

Radiologic stability in patients with MS requires that no new T1-gadolinium-enhanced lesions or expanding/new T2 lesions appear in the brain or spinal cord, a cornerstone of NEDA (no evidence of disease activity) concept in MS. If MAbs are being considered for therapy in the face of worsening disability, it can be a challenge since they do not penetrate the BBB.

Unlike nearly all other blood vessels in the body, the endothelial cells of the BBB are held together by tight junctions, and for a drug to enter the central nervous system (CNS), it must take the transcellular route. The tight junctions, coupled with numerous efflux transporters and metabolizing enzymes, constitute a barrier to the movement of both molecules and cells from the bloodstream into the CNS.
The BBB plays a role in MS treatment at multiple levels, and MAbs that have been listed herein cannot cross the BBB owing to their large size/molar mass or molecular size. The molar mass or the mass of one mole (6.02 x 10^23 molecules, Avogadro’s number) of the most commonly used MAbs in neuroimmunology, including those that are non-FDA approved are natalizumab (146 kDa), rituximab (143 kDa), alemtuzumab (145 kDa), ocrelizumab (148 kDa), and daclizumab (142 kDa), respectively. These data are critical since BBB penetration is inversely related to the square root of the molecular weight (or molar mass) of a substance; typically, few molecules >0.5 kDa cross the BBB.

There is minimal or no evidence that any of the MAbs impact neurodegeneration in a clinically relevant manner over the long course of MS, which is worrisome, particularly if MAbs are used as the sole therapeutic regimen. Additionally, the lipophilic or hydrophilic nature of molecules or size may not be the only limiting factors for drugs to cross the BBB.3

As patients transition into SPMS from RRMS, factors that drive the process include autoreactive T cells that cross the BBB and participate in demyelination, axonal transection, gliosis, and subsequent axonal degeneration4; the cascading neuroinflammation and neurodegeneration that follows continues unabated as the BBB forms an impregnable barrier to drugs. Additionally, memory B cells and plasma cells, central to humoral immunity, are found in lesions and cerebrospinal fluid (CSF) of patients with MS behind a protected BBB.

Ectopic lymphoid follicles located in the meninges probably drive the pathology of MS and have been shown to house B cells and plasma cells,5 indicating that B cells migrate to the brain and can be sustained locally within the CNS. Plasma cells do not carry CD20 cell surface molecules and are not affected by anti-CD20 MAbs. Although apparently restricted to late disease phases, the development of lymphoid tissue-like structures in brains of patients with MS suggests a pathophysiological role of B cells in MS that is possibly perpetual, eventually being one of the many contributors leading to SPMS.

The progressive phase of MS is an autoimmune disorder characterized by an intrathecal compartmentalization of inflammation resisting immunosuppressive treatments. The presence of lymphoid follicle-like structures in the meninges of some MS patients indicates that B cells can mature and perpetuate a compartmentalized humoral immune response.

If drugs are to act in the brain, CSF concentrations must be at least as high as in serum. As an example, the poor BBB penetration of IV rituximab became apparent in treatment of CNS lymphoma that produced concentrations that were 1000-fold less in CSF than seen in serum.6 Additionally, poor BBB penetration of IV rituximab was revealed in a study of 15 patients with MS that followed IgG levels, IgG index, and oligoclonal band numbers in CSF and noted that they were not consistently altered at 24 weeks; however, B and T cells in the CSF compartment were reduced although the mechanism remains unclear.7

The treatment landscape for MS continues to evolve. Impressive phase III data for ocrelizumab in clinical trials, OPERA I and OPERA II for RRMS, and ORATORIO for PPSMs, have been reported, particularly for disability scores. In the latter study, 24% reduced risk of clinical disability compared to placebo. The drug also reduced the time required to walk 25 feet by 29%, the volume of chronic inflammatory brain lesions by 3.4%, and the rate of brain volume loss by 17.5% compared to placebo. It is unclear how the beneficial effects on disability and MRI data on the brain occurred, given the size of the molecule and its poor penetration of the BBB, but certainly does not appear to be related to the phenomenon of “regression to the mean.”

Some illustrative examples of drugs—and this report makes no attempt to list all the possible combinations that can cross the BBB—are cyclophosphamide (CYC), an alkylating agent that penetrates the BBB, and CNS parenchyma, which has been shown to decrease pro-inflammatory T helper Th1 cytokine interferon-gamma and interleukin-12 in MS. It also increases the secretion of the anti-inflammatory Th2 cytokines IL-4 and IL-10 in CSF and peripheral blood.8 It suppresses cell-mediated and humoral immunity through its actions of T and B cells.9 Cyclophosphamide may be useful in advanced disease but has not been studied in a randomized clinical trial setting. It is perhaps time to revive an old drug.

Second, laquinimod, an investigational CNS-active immunomodulator and a small molecule, can diffuse freely across the BBB without any active transport, but cardiotoxicity at higher doses (1.2 mg/day) halted its progress in clinical trials and is clearly a limitation.10 Can it be used at lower doses that do not produce cardiotoxicity and yet be beneficial when combined with MAbs? That is a question only clinical trials can address.
Last, sphingosine-1-phosphate (S1P) receptors blockers cross the BBB but fingolimod failed in the PPMS study. However, the new S1P blocker such as siponimod has a relatively short half-life compared to fingolimod. It has fewer cardiac side effects and comes with BBB penetration capabilities. A phase III trial of siponimod in SPMS is ongoing. Could drugs such as CYC, fingolimod, or laquinimod be the future of MS therapies in combination with MAbs? Some other strategies that have been tried in oncology, for example, include the use of nanoparticles, immunoliposomes, peptide vectors, and design of influx transporters and could perhaps serve as model strategies for MS therapies moving forward.

The premise of this report lies in the fact that strategies to treat MS ought to begin early, before B-cell follicles have had time to develop. To address disease within the CNS, molecules that cross the BBB are critical. Alternatively, the best responsiveness to MAbs could perhaps be found in strategies that destroy encephalitogenic B-cell populations in the periphery at the clinically isolated syndrome (CIS) stage and not as second-line drugs.

The idea of combination therapy in MS is not new. Many studies have explored concepts such as safety, tolerability, and efficacy of several combination regimens but are underpowered and/or poorly designed. The key to success is to combine agents that have been shown to penetrate BBB with drugs that work effectively and show robust efficacy outside of the CNS, such as MAbs. For proof-of-concept studies, combination trials need to identify patients with worsening disability scores on EDSS, and selection of appropriate target population is key. Enrollment of failed RRMS patients on a standard drug based on NEDA criteria and whose EDSS is worsening perhaps forms the most eligible patient cohort to initiate combination therapy trials.

A seminal study analyzed immunological, histochmical, and morphometric data on post-mortem brain tissue samples from 29 SPMS and 7 primary progressive PPMS cases. B-cell follicles were detected in the meninges in 41.1% of the SPMS cases but not in PPMS cases, suggesting that the diseases are fundamentally different and treatment ought to begin at the RRMS or CIS stage of the disease. This strategy could be particularly useful for the AA patients with MS.

We will never know if combining a small molecule with MAbs at disease onset could work if we do not use scientific reasoning to address the disease mechanisms both inside and outside of the CNS. It must also be recognized that SPMS cases with follicles demonstrate younger age at onset, irreversible disability, death, and more pronounced demyelination, microglia activation, and loss of neurites in the cerebral cortex. Without addressing such fundamental pathological phenomena residing in a compartmentalized “zone,” MS therapies will continue to scratch the surface in treating worsening disability status in patients and fail summarily.

References

Teachable Moment

**Story From the Front Line**

D.H. is a healthy 58-year-old woman who went through menopause at 54, with the onset of hot flashes, vaginal dryness, forgetfulness, and frequent nighttime awakenings. She was offered hormone replacement for symptomatic relief shortly after the onset of menopause and because she has a uterus was put on combined conjugated equine estrogen (CEE) and medroxyprogesterone acetate. She has a total cholesterol of 212, a high-density lipoprotein of 43, and a family history of heart disease in a maternal aunt. She has also been treated long term with cabergoline for a prolactin-secreting pituitary adenoma, which is currently well controlled.

During the past year, she saw her internist who strongly recommended that she discontinue estrogen treatment secondary to concern for increased cardiovascular disease (CVD) risk. She was prescribed an herbal supplement and told to exercise more often. She is happily married and notes new onset of vaginal dryness, dyspareunia, and return of hot flashes and sleep disturbances since she recently discontinued her hormone replacement therapy (HRT). When seen for her refills for medications for her adenoma, she asked her reproductive endocrinologist, “Do I really need to stop taking estrogen?”

**Teachable Moment**

Myocardial infarction (MI) is the greatest risk for death in postmenopausal North American women. Data from over 30 observational studies have strongly suggested that estrogen is protective against heart disease. For example, the Nurse’s Health Study showed that ever users and current users had 0.5 (95% CI, 0.3–0.8, \( P = .007 \)) and 0.3 (95% CI, 0.2–0.6, \( P = .001 \)) relative risks (RR), respectively, for coronary disease compared to never users of menopausal hormonal therapy (HT). However, the Women’s Health Initiative (WHI), a large randomized controlled trial (RCT) aimed to address the effect of HT on CVD, breast cancer, and osteoporosis, discontinued the estrogen plus progestin arm because of lack of any demonstrable cardioprotective effect, excessive breast cancers (RR 1.26; 95% CI, 1.0–1.6), and an increased risk in the Global Index of Harm. The impact of these results was profound, with many women discontinuing their HT. However, when CEE was analyzed alone, the adverse effect on breast cancer virtually went away with a RR of 0.77 (95% CI, 0.6–1.0), but still there was a slight increased risk for all CVD (RR 1.12; 95% CI, 1.0–1.2).

In retrospect, the WHI was not designed to answer the question of whether estrogen can prevent heart attacks in newly menopausal women without heart disease. It enrolled older women (average age of 63) who were more likely to have advanced stages of atherosclerosis, supporting conclusions from the Heart and Estrogen/progestin Replacement Study (HERS) study, which suggested that HRT in women with known coronary artery disease might be at increased risk, at least in the first year of treatment.

With the passage of time since the landmark WHI study, there have been further re-analyses that suggested younger women on estrogen benefit disproportionately compared to older women. A 13-year follow-up of the WHI showed the group of women ages 50–59 at randomization who received CEEs had a 40% lower risk of MI than those who received placebo, whereas no effect was seen in women who were ages 60 or older at randomization. Furthermore, subsequent analyses from the WHI have shown the absolute risk of adverse effects (measured by the global index including stroke, pulmonary embolism, colorectal cancer, endometrial cancer, hip fracture, and...
The recently published ELITE (Early versus Late Intervention Trial with Estradiol) trial was specifically designed to test this hormone-timing hypothesis. This RCT stratified postmenopausal women into either early postmenopausal (<6 years) or late postmenopausal (≥10 years) groups and randomized them to receive oral estradiol (with vaginal progesterone if they had a uterus) or placebo. The primary outcome was the rate of change in carotid-artery intima-media thickness (CIMT) assessed by ultrasound every 6 months. After 5 years of intervention, the rate of CIMT progression in the early-postmenopausal group was significantly lower in the estradiol group than in the placebo group (absolute difference 0.0034 mm/year, \( P = .008 \)), whereas the rate of CIMT progression in the late-postmenopausal group was similar in the estradiol and placebo groups (difference 0.0012 mm/year, \( P = .29 \)).

The Global Consensus Statement on Menopausal Hormone Therapy, endorsed by the American Society for Reproductive Medicine and the North American Menopause Society, states menopausal hormone therapy (MHT) is the most effective treatment for vasomotor symptoms associated with menopause, particularly for women less than 60 years of age or within 10 years of menopause. Furthermore, randomized clinical trials and observational data have provided evidence that MHT may actually decrease coronary heart disease and all-cause mortality when initiated in women less than 60 years of age and within 10 years of menopause.

MHT should be considered as a safe option for symptomatic, healthy, early-menopausal patients, such as D.H., who should have the right to be involved in decisions about discontinuation of their HT regimens. Given the prevalence of heart disease in North America, if estrogen is a beneficial prevention tool, it deserves further research and dialogue between healthcare providers and their patients.

References

Choosing High-Value Care in Suspected Lower Extremity Deep Vein Thrombosis

Moon Won, DO, and Steven Connelly, MD

From the Department of Medicine, Greenville Health System, Greenville, SC (M.W., S.C.)

Clinical Scenario
A 70-year-old man with a past medical history significant for combined heart failure, chronic kidney disease stage 3a, type 2 diabetes mellitus, and prostate cancer (status postprostatectomy in 1996 and radiation in 2012) presented from a nursing home for altered mental status (AMS). Altered mental status was initially thought to be secondary to polypharmacy in the setting of new medication administration of Norco and Benadryl the night prior to presentation. At baseline, the patient ambulated independently and required no oxygen supplementation.

Upon exam, vital signs were stable except for requiring 2 liters of oxygen supplementation via nasal cannula to keep oxygen saturation >90%. Bilateral lower extremity (BLE) pitting edema (3+) to the knees and tightness were noted with mild tenderness to palpation bilaterally and without erythema. Bibasilar breath sounds were diminished. Cardiac exam was normal. Weight was 76 kg with a baseline weight of 72 kg. Initial abnormal labs included an elevated creatinine of 3.1 mg/dL, venous lactic acid of 4.2 mmol/L, brain natriuretic peptide of 1450 pg/mL, chest X-ray with cardiomegaly, and chronic bilateral pleural effusions.

Home medications furosemide and metolazone were initially held due to the elevated creatinine and lactic acidosis.

The patient’s AMS improved on day 2; his respiratory status, however, worsened and required 4 liters of oxygen supplementation. Bilateral lower extremity edema, tightness, and tenderness were noted to be worse. Home dose of furosemide and metolazone was restarted.

Treatment Options

Option A: Obtain BLE venous duplex with compression for worsening BLE symptoms to rule out an acute deep vein thrombosis (DVT). BLE venous duplex with compression for DVT was negative. Respiratory status and BLE symptoms improved with diuretics.

Option B: Obtain Well’s score: -2. Negative for active cancer, recent paralysis, paresis, or immobilization of lower extremities, recently bedridden, recent major surgery, localized tenderness along the distribution of the deep venous system, entire leg swollen, calf swelling of 1 lower extremity at least 3 cm larger than the other side, pitting edema confined to the symptomatic leg, previous DVT. Positive for an alternative diagnosis being more likely (decompensated heart failure). Low pretest probability for a lower extremity DVT; therefore, obtain a D-dimer: 0.15 mcg/mL (negative). Since the pretest probability is low and D-dimer negative, we can conclude that there is no DVT without obtaining a lower extremity venous duplex with compression study. Respiratory status and BLE symptoms improved with diuretics.

Discussion Questions

1. What is the initial approach to a patient with signs or symptoms of lower extremity DVT (ie, unilateral or bilateral lower extremity edema and/or erythema and/or pain)?

   a. Obtain lower extremity venous duplex with compression study
   b. Obtain a D-dimer
   c. Obtain pretest probability by using the Well’s score
**Answer:** Using the Well’s score for DVT to determine the pretest probability is the most important initial step. In patients with a low or moderate pretest probability (Well’s score of -2 to 2), a highly sensitive D-dimer test should be the initial test rather than a venous duplex with compression. In patients with a high pretest probability (Well’s score of ≥3), a venous duplex with compression should be the initial test.

2. What is the value of D-dimer in diagnosing a lower extremity DVT?

   a. Highly specific test to rule in a DVT
   b. Highly sensitive test to rule out a DVT
   c. Highly specific and sensitive test to rule in and rule out a DVT

**Answer:** D-dimer is a highly sensitive test to rule out a DVT but lacks specificity. There are multiple D-dimer assays available. According to Di Nisio et al, enzyme-linked immunofluorescence assay (ELFA), microplate enzyme-linked immunosorbent assay (ELISA), and quantitative latex assay had the highest sensitivities for DVTs with 97%, 95%, and 96% but had specificities of 42%, 47%, and 48%, respectively.\(^1\) A value <500 ng/mL or <0.5 mcg/mL fibrinogen equivalent units (FEU) has been frequently studied, but the cutoff value can vary by institution.\(^2,3\) D-dimer value <0.42 mcg/mL FEU is considered a negative value at Greenville Health System (GHS).

**Costs**

**Option A:** $508 for BLE venous duplex with compression

**Option B:** $27 for D-dimer

*Costs were obtained from heathcarebluebook.com.\(^4\) These costs are estimates and represent the amount typically paid by an insurance company.

**Teaching Moment**

The most frequently utilized initial diagnostic tool for a suspected acute lower extremity DVT at GHS is a venous duplex with compression. This approach is time consuming and very costly with a low positive yield. The diagnostic pathway recommended by American College of Chest Physicians (ACCP) and similarly by the National Institute for Health and Care Excellence (NICE) presents a cost-effective, safe, and easy-to-use guideline for clinicians to diagnose lower extremity DVT.\(^5,6\)

In patients who present with signs or symptoms of lower extremity DVT (ie, most commonly, unilateral or bilateral lower extremity edema and/or erythema and/or tenderness), the initial diagnostic test should be guided by the clinical assessment of pretest probability by utilizing the Well’s score for DVT. In patients with a low or moderate pretest probability (Well’s score of -2 to 2), a highly sensitive D-dimer test should be the initial test rather than a venous duplex with compression. In patients with a high pretest probability (Well’s score of ≥3), a venous duplex with compression should be the initial test.\(^5,7\)

D-dimer is a sensitive test but lacks specificity for the diagnosis of DVT and is, therefore, only useful when negative (ie, D-dimer value <0.42 mcg/mL FEU at GHS). A negative D-dimer level in conjunction with a low-to-moderate clinical probability of DVT is useful and cost-effective in excluding DVT without the need for an ultrasound examination.\(^8,9\) D-dimer values may be falsely elevated as a result of multiple factors: Most notably, the patient’s age (>60) and renal dysfunction were associated with false-positive D-dimer levels in 57% and 44% of venous thromboembolism-negative patients, respectively.\(^3,9\) Other factors that can lead to a falsely elevated D-dimer include recent surgery, trauma, pregnancy, and cancer.

There are multiple D-dimer assays available; at GHS, D-dimer is measured via the quantitative latex assay in mcg/mL FEU. According to Di-Nisio et al, ELFA, ELISA, and quantitative latex assay had the highest sensitivities for DVTs with 96%, 95%, and 93%, respectively.\(^1\) Another study by Bates et al showed that in patients with low-to-moderate pretest probability of DVT, a quantitative latex D-dimer assay reliably excluded DVTs.\(^10\)

**Intervention and Result**

We performed a retrospective review of all patients diagnosed with lower extremity pain, edema, or swelling who had a unilateral or bilateral lower extremity venous duplex with compression performed during their hospitalization at GHS’ Greenville Memorial Hospital between October 2014 and September 2015. The aim was to evaluate clinicians’ approach to patients with possible lower extremity DVTs and determine what measures could have been applied to provide a safe and most cost-effective work-up. Patients in the outpatient setting, surgical patients, pediat-
ric patients, patients with suspected pulmonary embolism, and patients with suspected upper extremity DVT were excluded.

Depending on the clinical assessment of pretest probability by utilizing the Well’s score for DVT, patients were categorized into groups of low, moderate, or high risk for a lower extremity DVT. Out of 68 total patients, 59 patients were categorized into the low-to-moderate risk group. Fifty-seven out of those 59 patients had a negative venous duplex with compression study. Ten out of the total 68 patients had undergone a D-dimer. Out of those 10 patients, 4 patients who were part of the low-to-moderate risk group had a negative D-dimer and had a negative venous duplex with compression study.

If all 59 patients in the low-to-moderate risk group had a D-dimer level drawn initially (as recommended by ACCP and per NICE guideline) instead of a venous duplex with compression study, a total of $25,506 could have been saved. During the same time frame, GHS (inpatient only) as a whole had a total of 218 venous duplex with compression studies (unilateral and bilateral) of the lower extremities ordered. Extrapolating the data from the study to the entire GHS, a potential total of $78,262 could have been saved.

Proposal: In patients who present with a suspected lower extremity DVT (unilateral or bilateral lower extremity edema and/or erythema and/or tenderness), the initial diagnostic test should be guided by the clinical assessment of pretest probability by utilizing the Well’s score for DVT.

In patients with a low or moderate pretest probability (Well’s score of -2 to 2), a D-dimer test should be the initial test rather than a venous duplex with compression study. If the D-dimer is negative (<0.42 mcg/mL), no further testing is recommended. If D-dimer is elevated above 0.42 mcg/mL, a venous duplex with compression study is recommended and, depending on those results, treatment can be started.

In patients with a high pretest probability (Well’s score of ≥3), a venous duplex with compression study should be the initial test. If positive, treatment can be started.

References


Research has established that members of particular demographic groups are inordinately burdened by differential healthcare access resulting from their race, ethnicity, social class, and geographic isolation.\textsuperscript{1,2} Given predictions that our society will become even more diverse in the next several decades, these health disparities will likely continue to be a challenge. To address differential healthcare access, many healthcare systems have introduced mobile health clinics (MHCs) to their mix of service delivery options. MHCs are defined as “transportable healthcare units that enable the provision of community-based care off-site from institutions and healthcare agencies to underserved populations that may otherwise be hard to reach.”\textsuperscript{3} That is, MHCs aspire to reach the more vulnerable populations that would otherwise have inadequate access to high-quality health care. Many MHCs often operate as an extension of larger healthcare systems to which patients are referred if they need additional services not addressed by a particular MHC.
MHCs have become increasingly common in the past decade; estimates indicate that 2000 such facilities provide services to 6.5 million people each year. MHCs provide a variety of preventive and primary care services, depending on available resources and on the particular community being served. Services include treatment of acute conditions (e.g., common cold, minor injury care, etc.) and chronic conditions (e.g., diabetes, hypertension, etc.); lab and diagnostic services; cancer screenings; specialty clinics; dental care; ophthalmology services; medication and prescription assistance; and health education. Over the past several years, MHCs have transitioned from addressing episodic, urgent healthcare needs to providing ongoing care to individuals with chronic conditions, a trend that is likely to increase in the future.

In fall 2015, the Department of Community Relations at Greenville Health System (GHS) funded and initiated a community assessment to determine residents’ attitudes and perceived needs pertaining to MHCs. This endeavor contributes to GHS’ efforts to expand access to health care via an MHC in Greenville County, SC. The research effort reported here consisted of 5 focus groups conducted in 5 underserved neighborhoods in Greenville County. The study results provide a starting point for the design, development, and delivery of MHC services to communities across the county.

Methods
The focus group methodology was used to ascertain residents’ general opinions about and preferences for an MHC. A hallmark of this methodology, which distinguishes it from the frequent, but inaccurate, label of “group interview,” is its encouragement of interaction among group members to elicit richer qualitative data about the topic under discussion. The dynamic nature of focus groups often brings information to the surface that would not otherwise emerge through other methods of research. The open-ended structure of focus groups allows researchers to learn what people feel about a particular issue, as well as how and why. In that respect, focus groups have several advantages over other forms of research, such as surveys, which generally collect individual responses to closed-ended questions that often do not allow for elaboration.

Sample Selection and Participant Recruitment
The GHS Institutional Review Board approved this study in October 2015. Purposive sampling was then used to select ethnically diverse, English- and Spanish-speaking women and men ages 20–67 who resided in 1 of 5 underserved neighborhoods in Greenville County, SC, at the time of the study. The 5 underserved neighborhoods were chosen based on areas of high risk and need for healthcare services and were selected as pilot sites for initial MHC delivery.

Participants were recruited through community centers, churches, community outreach representatives, community-based service provider liaisons, and GHS neighborhood health partners. Three days prior to the focus groups, study researchers contacted participants to remind them about the study. At the conclusion of each focus group, participants were provided with a $25 gas card. All individuals who volunteered to participate and who were scheduled for one of the focus groups ultimately participated in the study. The demographic characteristics of the focus group participants are summarized in Table 1.

Focus Group Delivery
The focus groups were held December 2015 at locations convenient to the participants, including community centers and churches. Each focus group had a main moderator, who led the focus group, and the principal investigator who took field notes throughout. Before starting any study-related procedures, participants were issued the informed consent. Each page of the informed consent was verbally read to them to ensure participants had a full understanding of the study. All participants provided written informed consent and completed a brief demographic questionnaire, providing information about background characteristics, current health status, and primary source of health care. Eleven questions were asked in the 5 focus groups. All 5 focus groups were audio recorded.

Data Analysis
The data analysis proceeded in several stages. First, a professional transcriber transcribed each focus group interview; each transcript was then verified for accuracy. The Spanish-speaking transcripts were transcribed to English by a GHS certified Language Services employee. One study investigator (C.M.) then engaged in more in-depth analysis, first reading each transcript in detail and writing initial analytic notes on emerging insights that guided the subsequent coding and analysis. The final transcripts were then uploaded into the qualitative software package ATLAS.ti (Version 1.0.49), an analytical tool that aided in the initial categorization and cod-
PERCEPTIONS/PREFERENCES FOR A MOBILE HEALTH CLINIC

ing of the data. Subsequent data analysis incorporated both deductive and inductive coding. The deductive analysis reported in this paper involved a more directed approach, guided by the interview protocol. Variables were coded according to the questions asked during the focus group. This coding was done to ensure that the primary research questions were addressed across all 5 focus groups. Then, using an iterative approach, these pre-existing codes were compared with the new codes and themes that emerged in the second stage of inductive analysis. (NOTE: Actual quotes from the focus group respondents appear in italics below.)

Results
Initial Perceptions of the MHC Model of Healthcare Delivery

The first main focus group question (“What is the first thing that comes to mind when you hear ‘mobile health clinic’? What images come to mind?”) served as an “ice-breaker” and allowed the researchers to learn about the participants’ general understanding of the MHC concept. Their responses provided a starting point for contextualizing participants’ more specific views about MHC service delivery.

A few participants were somewhat familiar with the concept of mobile healthcare delivery or had experience with similar healthcare offerings in the community. Some shared their perceptions about what an MHC looks like, comparing it to a local bloodmobile unit, a car that has a camper, a big bus that can care for people, a tour bus, and something mobile, that keeps moving, here and there, from one neighborhood to the next. Participants were aware that an MHC is not equivalent to a hospital and is not an operating room. However, they envisioned that the MHC facility would have the basic equipment necessary for offering general health care to the community. The MHC is viewed as a doctor’s office on wheels that comes with medicines, vaccinations for the kids, for people, for everybody.

Participants were aware that MHCs offer affordable health care for those who cannot generally pay to see a doctor through the traditional healthcare system; they perceived that an MHC would be less expensive than a hospital. Participants felt that this model of healthcare delivery is thus valuable to those in need of low-cost health care, especially for those who don’t have insurance and cannot afford to take [their children] to the doctor every time they got a scratch. Such a facility offers easy access for the people who really need it, if they come and take

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Demographic characteristics of focus group participants.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
<td>N</td>
</tr>
<tr>
<td>Gender, no. (%)</td>
<td>35</td>
</tr>
<tr>
<td>Female</td>
<td>28 (80.0)</td>
</tr>
<tr>
<td>Race/Ethnicity, no. (%)</td>
<td></td>
</tr>
<tr>
<td>African American/Black</td>
<td>24 (70.6)</td>
</tr>
<tr>
<td>Caucasian/White</td>
<td>2 (5.9)</td>
</tr>
<tr>
<td>Latino/Hispanic</td>
<td>8 (23.5)</td>
</tr>
<tr>
<td>Age, years (mean = 44.8), no. (%)</td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>7 (20.1)</td>
</tr>
<tr>
<td>30–39</td>
<td>8 (22.8)</td>
</tr>
<tr>
<td>40–49</td>
<td>6 (17.1)</td>
</tr>
<tr>
<td>50–59</td>
<td>5 (14.2)</td>
</tr>
<tr>
<td>60–69</td>
<td>9 (25.7)</td>
</tr>
<tr>
<td>Education, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Junior HS or less (1st-8th grade)</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>Some high school</td>
<td>6 (18.2)</td>
</tr>
<tr>
<td>Graduated high school or earned GED</td>
<td>9 (27.3)</td>
</tr>
<tr>
<td>Some college/technical school, no degree</td>
<td>10 (30.3)</td>
</tr>
<tr>
<td>2-year college degree</td>
<td>4 (12.1)</td>
</tr>
<tr>
<td>4-year college degree</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Employment, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Working full-time</td>
<td>5 (14.3)</td>
</tr>
<tr>
<td>Working part-time</td>
<td>8 (22.9)</td>
</tr>
<tr>
<td>Self-employed</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>A homemaker</td>
<td>6 (17.1)</td>
</tr>
<tr>
<td>Out of work for more than a year</td>
<td>2 (5.7)</td>
</tr>
<tr>
<td>Out of work for less than a year</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Retired</td>
<td>2 (5.7)</td>
</tr>
<tr>
<td>Unable to work</td>
<td>10 (28.6)</td>
</tr>
<tr>
<td>Income, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Less than $10 000</td>
<td>16 (47.1)</td>
</tr>
<tr>
<td>$10 000–$19 999</td>
<td>9 (26.5)</td>
</tr>
<tr>
<td>$20 000–$29 999</td>
<td>2 (5.9)</td>
</tr>
<tr>
<td>$30 000–$39 999</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>$80 000–$89 999</td>
<td>2 (5.9)</td>
</tr>
<tr>
<td>Choose not to answer</td>
<td>2 (5.9)</td>
</tr>
</tbody>
</table>

Note: Not every focus group respondent answered every item on the questionnaire.
MHCs were viewed as convenient, situated in a central location in the community, thus offering quick and easy access to health care. As a model of mobile sufficient care, MHCs are important because some people ... may need some [non-emergency] help. And by the bus being in the community, they may be able to get there quicker and to receive the help they need at that time. This point is especially important for individuals lacking transportation and for those whose busy and complex schedules make it difficult to visit healthcare professionals in other locations. Thus, participants envisioned that an MHC would have a predictable schedule: I imagine that the doctors come on a certain day, certain time, to a place that is conditioned to give care. Patients would thus be able to get an appointment to go there at a certain time and get out fast.

Related to convenience, accessibility (local health) was an additional key characteristic. This more specific factor refers to the ease of seeing a particular doctor. As one participant indicated, the presence of the MHC would be much like having a workplace nurse that offers "on-the-spot" diagnosis at places of employment. In the words of one participant, the nurse could say "you need to be seen right now. You need to go to the emergency room." [As a result, at an MHC], at least you could be told the seriousness of your situation, if it is serious. Thus, the MHC is also where residents can get emergency treatment, especially if they cannot see their regular doctor and the MHC happens to be in the community at the time that they need such care.

Prior Experiences With the MHC Model of Healthcare Delivery

To learn more about participants’ views on MHCs, participants were asked to describe their prior experiences with this model of healthcare delivery. Several participants indicated they had visited a local bloodmobile unit and remarked on several positive qualities of this facility, including cleanliness (You wouldn't be afraid that you would catch something or be contaminated by; It's obviously very clean); attractiveness (It's very visible and showy; You can't miss it); convenience (You don't have to have an appointment); comfort (It's not like it's small in there); safety; and the well-qualified staff who know what they're doing. Because the local bloodmobile unit has a substantial and known presence in the community, residents seem to trust the care it offers.

Some individuals reported they had visited a mobile dental health clinic in the community. Another participant visited a mobile health facility offered by a local hospital at a local church. In this instance, the participant described receiving mammograms and other women-centered services through this healthcare modality. This participant was impressed with the convenience, the quality of services provided, and the friendly and attentive staff: I arrived and they provided me with a great service, because they are very nice people, the ones there. Then, I had some tests done and it was fast. I don't have a reason to lie to you. They didn't take a long time. I even went, "Wow, this is faster than the hospital." Another participant, who volunteered at the MHC sponsored by a local hospital, described the facility as beautiful, state-of-the-art and the staff as wonderful, very friendly, and very much oriented to outreach. She said that she couldn't imagine someone hesitating to want to have any kind of health care on that bus.

Nearly all of the participants in one focus group indicated they did not have prior experience with an MHC. Similarly, participants in another focus group indicated that they had no prior experiences with MHCs. However, when prompted, they said they were familiar with the local bloodmobile unit.

When asked about their initial perceptions of MHCs, several participants provided examples of health care offered through other kinds of entities, such as stand-alone facilities and a logistic transport service. Although not directly comparable to MHCs, the responses offer insights into the characteristics that should be considered when offering MHC services. One participant reported having a negative experience with a dental clinic offered through a community-based health clinic offering medical services to community members at no cost. She said she waited in line for a long time for this first-come, first-served service; due to the long wait, though, she ultimately had to be rescheduled for the next day.

Perceptions of MHC Delivery in Participants’ Own Neighborhoods

After providing information about their initial perceptions and prior experiences with the MHC model of health care, participants were asked several more specific questions: “What do you think about health services provided on a
I've got to say, I would love it! That's all. As one participant said, I would love it! That's all I've got to say. I would love it.

Another participant indicated she would feel comfortable and grateful, especially given that she faces language barriers when obtaining health care through a hospital. Participants felt they could gain access to a variety of services through MHCs and thus expressed that an MHC would be valuable to children, teens, elderly, and the disabled alike. In the words of one participant: I have to take my son to the doctor when he has a problem ... and make sure he's fine. But then in the long run, I don't worry about myself. I just make sure my child is OK.

Another participant recognized that the MHC would be an asset for those people who won't or can't get out and that would otherwise not get treatment, perhaps because they are not able to, cannot afford it, or resist going to the doctor. For example, one participant indicated that she often cancels her regular doctor's appointments: I say, "I've got a doctor's appointment. I don't want to go."... [then] I might call and cancel and then go the next time. However, she indicated that if the MHC came to her neighborhood, she would take advantage of its services. Another participant corrected the assumption that an MHC only benefits very poor community residents, saying that it would benefit a lot of people with different incomes, different background[s]. She continued by saying a lot of people always think it's just about somebody who does not work or [is] just poor or homebound ... but it really helps people like me. I'm working class and ... self-employed. So, health care for me would be very, very expensive. So stuff like this really helps.

The easily accessible health care available through an MHC is very important to participants who feel that the MHC would likely curb visits to the emergency room. Also, participants perceived that they would not have to wait as long to see a doctor at an MHC as they would at a hospital or at a regular doctor's office. In the words of one participant: It would be just as good or valuable to you as being seen in a doctor's office, where you may wait 2 hours and then see a nurse practitioner. Another participant noted that many people feel like they have to wait for a long time when they see a regular doctor, and they don't have time to go, or don't want to go, so a lot of people get neglected by not going. Thus, convenient scheduling is another important characteristic of a neighborhood-based MHC. Maybe they will give you an appointment ... You can go home and come back at the time they gave you, and this makes it more accessible.

Although participants felt positive about the MHC coming to their neighborhoods, some noted that patients who access health care through an MHC may be stigmatized by their fellow community members, most probably because the MHC itself would have such a visible presence in the community (eg, community residents may see others waiting in line for MHC services): I think some people would be ashamed to use it because [of the perception that it's] for homeless people, or people who can't afford to get in. Such individuals may be embarrassed to use an MHC due to their strong sense of pride.

Others indicated that such stereotypes would not prevent them from seeking health care through an MHC: It's [about] my health, and if it can help me, I don't care what's going on or what's being said ... I will take care of myself. Another indicated he wouldn't care what people think. I'd be glad to use it. Another participant felt that some community members would have mixed thoughts about the MHC given that it would be a new entity in the community: There's going to be a segment of the population that will receive it very well, and I think there will be some people that will be hesitant to think it's a good thing. But that's just different mindsets and different generations ... [and] the way they deal with anything new. It takes time for them to accept.

Preferences Regarding Types of Services Offered through the MHC

Participants offered a variety of suggestions for the services that could be offered through the MHC, ranging from basic “wound care” to comprehensive total care ... anything that does not require surgery. They indicated that an MHC could treat...
both acute conditions (such as the flu) to more chronic conditions (such as asthma). At the same time, participants were realistic in their expectations, recognizing that there are certain things you can’t take care of on a bus or a mobile clinic.

Across all 5 focus groups, the most commonly requested service was for basic preventive care and a general check-up. As such, participants envisioned that the MHC would offer physical exams, during which the patient could receive a series of lab services and tests, such as blood pressure checks, cholesterol tests, pregnancy tests, and diabetes tests. They would like to receive wound care, plus treatment for fever, colds, and strep throat along with flu shots and X-rays. A few participants specified a need for basic ophthalmic and dental care (eg, checkups, dentures, etc.). They also felt it was important that the MHC have the ability to fill and refill prescriptions and that such prescriptions should be affordable: We know that we need some type of medicine, and then if we don’t have insurance, we have to pay out of pocket for that medicine and things like that. Most medicines I get from the emergency room, my prescription is $50 and above, and … I [don’t] always have the money to pay for it. Easy access to prescriptions was especially important in one of the communities where many residents do not have transportation and where there is no drugstore in the community.

In terms of more specialized care, several participants requested a variety of oncology services, including basic cancer screening, mammograms, and colonoscopies. Several women expressed a desire for OB/GYN care and pediatric services on the MHC. Participants hope that the MHC can offer specialized services for men. As one participant indicated, the work for men here is so arduous, so hard. Another participant stated that the men don’t eat well and they work too much, a lot of physical effort.

Participants envisioned that the MHC would be able to offer basic emergency “triage” care and then transport patients to the hospital, if necessary. Similarly, they felt it was important that the MHC staff be able to refer patients to other doctors for further care, if necessary, and to send us to the appropriate doctor that we need. Because sometimes we don’t know if it is a nutritionist, a psychologist, neurologist, psychiatrist … We don’t know. In cases where a patient would need to be referred to another facility, participants requested that the MHC staff advise them about affordable alternatives for the additional health care. As a participant noted: I don’t have health insurance. [Every year], I go to a private doctor’s office … he orders labs [tests and] sends me to a lab. That lab has an agreement with the doctor’s office, and they give a big discount to that doctor so I can have my labs done there. She would like similar arrangements to be available through the MHC.

Some participants see the MHC as a conduit for offering health education to residents; a participant suggested that patients could benefit from nutrition education, dietary services, and advice about exercise. In the words of another participant: Doctors give you a lot of stuff, but they don’t tell you why. They don’t say, “You know, if you eat more of this, you can stop taking this pill.” … They tell you to diet, but you know, [there are] all kind of diets out there that are bad for your health.

Beyond obtaining general healthcare services, participants would also like to be able to access information about other services available in the community, to have the opportunity to talk to a social worker, to be able to see a doctor who could diagnose both physical and emotional causes (eg, stress) of illness, and to receive advice about payment plans. Several participants hoped the MHC would also offer a few “extras,” including bathrooms, blankets (to keep people warm while they wait), toys, and a waiting room (both for the participants who may be visiting the MHC and their children). The facility should also be handicapped accessible, prioritize persons with disabilities, and have bilingual staff on hand.

Preferences Regarding the Schedule of MHC Services

Participants had a variety of opinions about the preferred days and hours of MHC services, ranging from twice a week to once a month. Although most preferred that the MHC visit at least once a week, they also recognized this option could be difficult. But even once a month would be preferable and would be better than nothing at all, because this is really needed; twice-a-month visits would be ideal. As one participant remarked, however, consistency of service was even more important than actual frequency. Such consistency would be a way for the MHC staff to show they cared about the community.

Regarding the preferred days of the week for MHC services, several participants preferred weekend hours; participants indicated that both Saturday and Sunday would be convenient for community members. However, it would be nearly impossible for many residents to attend on Saturday due to...
childcare duties; thus, they preferred visiting the MHC during the week, when their children are in school. In addition, several female participants indicated that Saturday and Sunday hours would be ideal for the men in the community as it is very difficult for them to attend the MHC during the week (without taking unpaid leave from work).

Preferences Regarding the Location of the MHC
Regarding the ideal location for the MHC, participants offered suggestions based on their geographic locations. For example, participants in one focus group suggested the MHC rotate around a particular community so more residents could avail themselves of the clinic’s services. The suggestion was also made to locate the MHC at a church so that healthcare services could be offered on the van and in the church, if necessary. Wherever the MHC is eventually located, several participants indicated that the MHC must be located in a safe area of the community: And I think people probably would trust, would feel safe going to an area where the churches are versus the outskirts of the community that are maybe perhaps not perceived as safe.

Limitations
As the study relied on a small, purposefully selected sample, the focus group results should not be generalized to the population within each of the 5 communities included in the study or to Greenville in general. Rather, the findings of the focus groups represent both the opinions of the particular individuals who participated, as well as additional opinions and viewpoints that may have taken form as a result of participating in the focus group.8

It is also possible that individuals who participated in the focus groups may have already been predisposed, one way or another, toward the concept of MHCs, and thus began the focus group with a strong bias about MHCs. However, that does not seem to be the case with this study as only a few participants had prior knowledge about or experience with MHCs. Although the focus group format capitalizes on a social context that encourages participants to reflect on one another’s ideas, it may also limit the information any one participant can share, inhibit the expression of minority opinions, or limit the participation of individuals who are not particularly confident or articulate. Some individuals may not have expressed their full opinions because of concerns about the confidentiality of what they say in a group setting such as the focus group. It is also possible that some of the rich data and cultural nuances may have been lost when the Spanish focus group’s comments were translated into English.

Discussion
Our study used the focus group methodology to more effectively capture the variety of opinions about MHCs in Greenville County. The 5 focus groups provide important insights into residents’ opinions about MHC healthcare delivery. Importantly, all 5 focus groups included community residents who are generally disenfranchised from the traditional healthcare system (ie, by virtue of social class, race/ethnicity, geographic isolation, etc.) and thus often do not have the opportunity to express their opinions regarding healthcare delivery. We believe that the focus group methodology holds promise for assessing future community health needs and community interest in health programs and should be considered in the design of any future community health assessments.

In all 5 Greenville groups, the most commonly requested service was for basic preventive care and a general check-up; health education was suggested as a way to provide this preventive care. Other researchers agree that services needed include health promotion and disease prevention,5,8,10 instead of focusing on curative services.5 Based on the results of the focus groups, it is recommended that the MHC provide health promotion and preventive services and consider providing health education. Additionally, although there were differing opinions about the frequency of MHC visits to communities, participants across all 5 focus groups indicated that consistency and predictability were also important. This finding reinforces Campos and Olmstead-Rose’s research that emphasized the need for an ongoing provider-patient relationship in the context of MHC services.5

Across all 5 focus groups, participants generally felt very positive about the possibility of obtaining personalized health care through an MHC unit that would visit their own neighborhoods. Participants prefer MHCs to be convenient, situated in a central location in the community, thus offering quick and easy access to health care, and valuable to those who need low-cost health care. Other research studies report that MHCs, more than being geographically convenient, are perceived as offering services that are acceptable, user-friendly, and accommodating to vulnerable populations.3,5,8,10
Conclusion

This MHC presents an exciting opportunity for GHS to provide health care to underserved and vulnerable populations in Greenville County. Overall, participants had somewhat limited experiences with obtaining general health care through an MHC, although several reported familiarity with the MHC model (similar to that provided through the local bloodmobile unit) and others reported receiving specialized care through MHC-type facilities. Those who reported receiving such services through these facilities felt positive about the experience. Participants stressed the importance of the MHC to offer services with kindness and respect in a clean, safe, and confidential environment.

It is critical for healthcare providers and health systems to understand the needs of underserved communities prior to the launch of healthcare delivery projects and to ascertain the level of community readiness and acceptability. Across all 5 focus groups, participants had favorable opinions about the possibility of obtaining personalized health care through an MHC unit that would visit their own neighborhoods.

Participants desire sustainability and consistency of mobile health delivery services. Participants are especially interested in receiving preventive health care through the MHC, including health education. Thus, health systems may want to consider providing primary health care at the beginning of the MHC delivery initiatives and then consider additional services and programs as they learn more about the community. This process will allow health systems to better meet community members’ primary healthcare needs and to develop an MHC that reflects the unique character of each community.

Using focus groups for community needs assessment is a powerful method for determining attitudes and perceived needs because information comes to the surface that would not otherwise emerge through other methods of research. In this study, the researchers, using focus group methodology, were able to successfully conduct a community assessment which determined that groups of residents in underserved communities expressed a desire and readiness for the MHC. Their enthusiasm was exhibited by their questions regarding the MHC start date.

References

4. Song ZC. Mobile clinic in Massachusetts associated with cost savings from lowering blood pressure and emergency department use. Health Aff. 2013;32:36-44.
Although the science and practice of medicine evolves daily, the basic model of the 4-year medical school curriculum in the United States has seen little change since the Flexner Report. The transition from medical school to residency has become an increasingly difficult one for today’s medical graduates. Of primary concern is the fourth year of medical school (M4), which has been described as a year lacking direction and missing an opportunity to better train students to transition into their internship year. Numerous general surgery residency programs have addressed the perceived laxity of the M4 year with a “boot camp” for senior M4 students entering a surgical specialty. Participants have described these camps as the most beneficial portion of medical school in preparation for their internship year, reporting an increase in their

The Gynecology and Obstetrics Fundamentals of Residency Internship Training (GO FOR IT) Trial

Francis S. Nuthalapaty, MD; H. Lee Higdon III, PhD; David A. Forstein, DO; Sarah E. Smith, MD; Julie Z. DeCesare, MD; Claudette J. Shephard, MD; Robert V. Higgins, MD; Chadburn H. Ray, MD; Ashlyn H. Savage, MD; Nikki B. Zite, MD, MPH; Spencer G. Kuper, MD; and Brian C. Brost, MD

From the Greenville Health System/University of South Carolina School of Medicine Greenville, Greenville, SC (F.S.N., H.L.H., D.A.F.); East Carolina University Brody School of Medicine, Greenville, NC (S.E.S); Florida State University College of Medicine Program, Pensacola, Fla (J.Z.D.); University of Tennessee Health Science Center, Memphis, Tenn (C.J.S.); Carolinas Medical Center, Charlotte, NC (R.V.H.); Georgia Regents University, Augusta, Ga (C.H.R.); Medical University of South Carolina, Charleston, SC (A.H.S.); University of Tennessee Medical Center at Knoxville, Knoxville, Tenn (N.B.Z.); University of Alabama at Birmingham, Birmingham, Ala (S.G.K.); Wake Forest School of Medicine, Winston-Salem, NC (B.C.B.)

Abstract

Background: Boot Camps, condensed format courses that emphasize procedural skills and medical knowledge, are a common, but unproven approach to helping prepare fourth-year medical students (M4) for residency.

Methods: This multicenter quasi-experimental static group educational study involved M4 students from 8 ACGME accredited residency programs. Participants were assigned to either the intervention (GO FOR IT) or control groups based on availability to attend a training course in April 2013. Course activities included lectures and simulation-based procedural skills practice. End-of-study competency assessments were conducted June 15–July 2, 2013. The primary study outcome was the composite score of 13 assessments, including objective-structured clinical exams, technical skills performance checklists, and knowledge assessments.

Results: Thirty-two of 42 (76%) possible students enrolled in the study, of which 11 were assigned to the GO FOR IT group and 21 to the control group. The median composite end-of-study assessment score was 73% in the GO FOR IT group as compared to 41% in the control group (P < .001).

Conclusions: Participation in an intensive 2-week postresidency-match M4 elective resulted in significantly greater scores in the assessment of clinical and procedural skills and medical knowledge as compared to the usual activities students pursue at the conclusion of medical school.
self-confidence about being a surgical intern, an enhanced self-perceived dexterity, surgical skills, and ability to safely manage patients. 6-8

Limitations of these preliminary investigations are their narrow focus on skills sets necessary for a general surgery residency and their reliance on learner self-assessment as a primary outcome, which do not provide objective evidence to support whether such interventions truly impact the competency of M4 students preparing for an OB/GYN (Obstetrics and Gynecology) internship. The objective of this study was to determine the impact of participation in an intensive 10-day postresidency-match M4 electve, compared to usual activities, on clinical, procedural, and knowledge competencies assessed at the time of matriculation into an OB/GYN internship.

Methods

The Gynecology and Obstetrics Fundamentals of Residency Internship Training (GO FOR IT) Trial was a multicenter educational study involving 8 Accreditation Council for Graduate Medical Education (ACGME) OB/GYN residency programs in the southeastern United States. Study conduct was separated into 5 sequential phases. Phase 1 (collaborative and curriculum), from October 2011 to September 2012, involved formation of the GO FOR IT trial collaborative and determination of the curricular content and assessments. All ACGME-accredited OB/GYN residency programs within a 300-mile radius of the primary study center (PSC) were identified and their program directors contacted to assess interest in joining the study collaborative. Of 23 possible programs, 8 joined the collaborative. This study was approved by the Institutional Review Board of Greenville Health System (IRB#Pro00014309), which served as the PSC and Data Coordination Center (DCC). Each site also obtained study protocol approval. All site principal investigators (PI) participated in mandatory web-based and in-person training on study procedures.

Twenty-four medical knowledge (Table 1) and 12 clinical/procedural learning outcomes (Table 2) were selected from the report of the Association of Professors of Gynecology and Obstetrics/Council on Resident Education for Obstetrics and Gynecology Joint Task Force on Milestone One. 9 De novo assessments were designed for each of the 12 clinical/procedural learning outcomes. Site PIs developed a performance checklist and standardized simulation scenario (if needed). Each assessment tool was then submitted for review to 2 other site PIs to ensure content validity. A list

<table>
<thead>
<tr>
<th>Learning Topics</th>
<th>Teaching Method(s)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gynecology</strong></td>
<td></td>
</tr>
<tr>
<td>Evaluation and management of abnormal first-trimester pregnancy, including ectopic</td>
<td>DL</td>
</tr>
<tr>
<td>Pathophysiology, evaluation and management of reproductive tract malignancies</td>
<td>DL</td>
</tr>
<tr>
<td>Evaluation of acute pelvic and lower abdominal pain</td>
<td>CBL</td>
</tr>
<tr>
<td>Pathophysiology and evaluation of abnormal uterine bleeding</td>
<td>DL, CBT</td>
</tr>
<tr>
<td>Indications and alternatives for hysterectomy</td>
<td>W</td>
</tr>
<tr>
<td><strong>Obstetrics</strong></td>
<td></td>
</tr>
<tr>
<td>Physiologic adaptations of pregnancy and the puerperium</td>
<td>CBL</td>
</tr>
<tr>
<td>Evaluation and management of third-trimester bleeding</td>
<td>CBL</td>
</tr>
<tr>
<td>Pathophysiology and management of preterm labor</td>
<td>CBL</td>
</tr>
<tr>
<td>Electronic fetal heart rate interpretation</td>
<td>CBT</td>
</tr>
<tr>
<td>Indication and interpretation of antenatal fetal testing</td>
<td>DL, CBT</td>
</tr>
<tr>
<td>Conduct of postpartum care, including breastfeeding and contraception</td>
<td>W</td>
</tr>
<tr>
<td>Pathophysiology and management of gestational hypertensive disorders</td>
<td>CBL</td>
</tr>
<tr>
<td>Management of diabetes mellitus during pregnancy</td>
<td>CBL</td>
</tr>
<tr>
<td>Management of common antepartum complications</td>
<td>CBL</td>
</tr>
<tr>
<td>Management of spontaneous abortion</td>
<td>CBL</td>
</tr>
<tr>
<td>Counseling for aneuploidy screening</td>
<td>CBL</td>
</tr>
<tr>
<td>Evaluation and management of postpartum hemorrhage</td>
<td>CBL</td>
</tr>
<tr>
<td>Pathophysiology and management of postpartum fever</td>
<td>CBT</td>
</tr>
<tr>
<td><strong>Office practice</strong></td>
<td></td>
</tr>
<tr>
<td>Content and conduct of routine well-woman care</td>
<td>DL</td>
</tr>
<tr>
<td>Evaluation and management of urinary tract, vaginal, vulvar, and sexually transmitted infections</td>
<td>DL, CBT</td>
</tr>
<tr>
<td>Contraceptive methods, indications, contraindications, and complications</td>
<td>DL</td>
</tr>
<tr>
<td>Evaluation and screening of breast disease</td>
<td>W</td>
</tr>
<tr>
<td>Options and counseling for undesired pregnancy</td>
<td>W</td>
</tr>
<tr>
<td>Evaluation and management of the abnormal Pap smear</td>
<td>DL, CBT</td>
</tr>
</tbody>
</table>

*Key for teaching methods: DL = didactic lecture; CBT = computer-based training module; W = live webinar. All topics were presented in a 30-minute learning session. Self-directed CBTs were optional and of variable length.
of the learning outcomes, associated teaching/learning tools, and assessments was compiled into a website for on-demand use.\textsuperscript{10}

Phase 2 (recruitment and enrollment) began in October 2012 and involved site PIs presenting information about the study to M4 students during their residency interview. Enrollment commenced on Match Day 2013. Eligible subjects were those who participated in the 2013 National Residency Matching Program and matched into one of the collaborative centers. Additionally, subjects had to be available to relocate to the PSC/DCC from April 15−26, 2013. Participants who were unavailable or unwilling to complete the end-of-study competency assessments were excluded from the study. All M4 students who matched into one of the collaborative programs were sent electronic and hard copy documents, which included a formal invitation to participate in the study, the study brochure, and consent form. All potential participants were then contacted by phone to complete the consent process.

Phase 3 (assignment) of the study consisted of a study group assignment contingency plan due to the uncertainty of student availability. Not enough students were available to relocate to accomplish the randomization scheme, so the contingency plan was activated resulting in a quasi-experimental static group design.\textsuperscript{11-13} Educational research differs from clinical research in both design and nomenclature. Quasi-experimental studies are analogous to observational studies of clinical research.\textsuperscript{13} A PubMed search of “quasi-experimental design” reveals well over

<table>
<thead>
<tr>
<th>Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technical learning outcomes and associated teaching and assessment methods.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Learning Outcomes</th>
<th>Teaching Method(s)*</th>
<th>Assessment Method*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical/Procedural skill</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comprehensive women's health history</td>
<td>CBT</td>
<td>Standardized patient OSCE with 55-item performance checklist completed by proctor via direct observation</td>
</tr>
<tr>
<td>Breast and pelvic exam</td>
<td>TT, CBT</td>
<td>Standardized patient OSCE with 37-item performance checklist completed by proctor via direct observation</td>
</tr>
<tr>
<td>Two-handed knot-tying</td>
<td>TT</td>
<td>Bench model with visual inspection of completed knot by proctor</td>
</tr>
<tr>
<td>Intrapartum cervical assessment</td>
<td>TT</td>
<td>Soft cervical models within blinding chamber (5 items) with assessment of both dilation and effacement</td>
</tr>
<tr>
<td>Normal vaginal delivery</td>
<td>TT, SS</td>
<td>Simulation scenario using pelvic delivery model; proctor serves as standardized patient and completes 23-item procedural checklist immediately following completion of scenario</td>
</tr>
<tr>
<td>2nd-degree vaginal laceration repair</td>
<td>TT</td>
<td>Bench model with 12-item procedural checklist completed by proctor via direct observation</td>
</tr>
<tr>
<td>Intrauterine device insertion</td>
<td>TT, CBT</td>
<td>Bench model with 12-item procedural checklist completed by proctor via direct observation</td>
</tr>
<tr>
<td>Endometrial biopsy</td>
<td>TT, CBT</td>
<td>Bench model with 12-item procedural checklist completed by proctor via direct observation</td>
</tr>
<tr>
<td>Vaginal wet-prep interpretation</td>
<td>CBT</td>
<td>6-item computer-based assessment</td>
</tr>
<tr>
<td>Technical knowledge</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical instrument name and principal use</td>
<td>HO, CBT</td>
<td>30-item computer-based assessment with high-resolution photographs</td>
</tr>
<tr>
<td>Surgical suture, blade, and needle types</td>
<td>HO, CBT</td>
<td>18-item assessment with sutures, blades, and needles identified by direct visual inspection</td>
</tr>
</tbody>
</table>

* Key for teaching and assessment methods: CBT = computer-based training module; TT = task trainer; SS = simulation scenario; HO = hands-on use; OSCE = Objective Structured Clinical Exam. Individual skills learning sessions were 30 minutes in length and offered varying frequencies dependent on learner needs. All skills learning sessions totaled 50 hours. Self-directed CBTs were optional and of variable length.
4500 peer-reviewed publications utilizing this study method.14

Phase 4 (intervention) commenced April 6, 2013. All subjects completed a baseline demographics questionnaire and a self-assessment of perceived competency in knowledge and procedural skills. Subjects assigned to the intervention group relo-
cated to the PSC/DCC from April 15–26, 2013. The first day of curriculum exposure for the GO FOR IT group included a half-day baseline skills assessment followed by an individual debrief ses-

sion. Each of the subsequent 8 days followed a template of three 0.5 hour didactic sessions and then 6 hours of simulation-based procedural skills practice. A novel technique for longitudinal simulation-based training developed by one of the investigators (B.C.B.), the Procedural Repetition Involving Montessori-type Experience and Rehearsal (PRIMER) Method (Fig. 1), was utilized. The last day of the GO FOR IT course included an individual debrief session followed by a final skills assessment. During the intervention phase, there was no contact with the subjects in the control group, except to schedule activities for Phase 5.

Phase 5 (assessment) spanned June 15–July 2, 2013. All subjects were required to schedule and complete the National Board of Medical Examiners (NBME) OB/GYN Subject Exam at a commercial testing center (Prometric, www.prometric.com). All subjects were also required to report to 1 of 5 collaborative centers to participate in the standardized end-of-study assessments. This assessment included Objective Structured Clinical Exam (OSCE) stations, technical skills procedural checklist stations, and technical knowledge stations (Table 2). The assessments were grouped into 7 stations, each 15 minutes in length and video recorded.

The primary outcome for the study was the median composite score of all end-of-study assessments (excluding the NBME subject exam). Secondary outcomes included the individual OSCE and procedural checklist scores and the NBME subject exam percentile score. All OSCE procedural checklist stations were scored immediately at the testing center by the site PI. All other stations were scored post hoc at the DCC either by video review or grading of the answer form. All scoring forms were returned to the DCC and the data entered into Research Electronic Data Capture15 and then exported to SPSS (IBM Inc., Armonk, NY) for analysis.

The sample size calculation for this study was based on a traditional two-group superiority testing approach. The primary outcome was estimated to be 80% in the GO FOR IT group and 64% in the control group with a standard deviation of 15%. The alpha was set at .05 with a desired power of 80%. Using a two-tailed test, the resultant sample size calculation was 15 subjects per group. The statistical plan for secondary outcomes utilized a similar testing approach with the alpha set at .05. The statistical analysis was blinded and based on an intention-to-treat principle. Due to group size, statistical testing required a non-parametric approach. Results are reported as median percentages with the 25th and 75th percentiles. The Wilcoxon rank sum test and Fisher’s exact test were used to analyze continuous and categorical variables, respectively. A P value < .05 was considered statistically significant.
Results
On March 15, 2013, 42 M4 students matched into the 8 study collaborative residency programs. Eleven students met all study criteria and were placed into the GO FOR IT group; 21 students met all criteria except the ability to relocate to the PSC and were thus placed into the control group. Ten students declined to participate (Fig. 2). Ultimately, 32/42 (76%) of potential students participated in the trial. There were 4 instances of protocol deviation following group assignment. Three subjects in the control group failed to complete the baseline questionnaire and 1 subject in the control group chose not to complete the NBME OB/GYN Subject Exam.

There were no differences between the GO FOR IT group and control group in regard to age, United States Medical Licensing Examination results, or time spent in OB/GYN clinical activities in the M3 year, but the control group did report more weeks spent in OB/GYN clinical activities in the M4 year (Table 3). The control group had a higher median self-rated competency score in two-handed knot-tying and normal vaginal delivery, as compared to the GO FOR IT group, but all other self-rated competency scores were similar between groups (Table 3).

The median composite end-of-study assessment score was 73% (68%, 77%) in the GO FOR IT group as compared to 41% (35%, 45%) in the control group ($P < .001$). Similarly, the GO FOR IT group scored significantly higher than the control group on 10 of 13 end-of study competency assessments (Table 4).

Discussion
In July 2014, the ACGME implemented Milestones for the Obstetrics and Gynecology specialty, which defined an explicit set of competency-based developmental outcomes that can be demonstrated progressively by residents and fellows from the beginning of their education through graduation to the unsupervised practice of their specialties.16 This study provides objective evidence regarding the extent to which a short, intensive course of knowledge and skills training prior to medical school graduation can impact clinical competency at the very beginning of the Milestones continuum.

There are several key implications of this study. First, while the curriculum addressed medical knowledge and procedural skills competencies, the findings suggest that the curricular format had the greatest impact on procedural skills. This finding may be a result of participants having less procedural competency at baseline as compared to medical knowledge and thus more to gain through the procedural training. Alternatively, either the scope or approach used in addressing the knowledge competencies in this curriculum was not effective. Second, it is important to note that the effect on the procedural competency was sustained over 8–10 weeks between training and final testing. This finding suggests offering such training at the end of the M4 year is an alternative to delaying such training until residency. Finally, our study demonstrates how reliance on student self-perceived competency can be misleading, and a primary limitation of prior studies.

Several characteristics of this study enhance the strength of its findings. First, the multicenter design ensured a heterogeneous study population. Participants came from 18 medical schools, had a variety of clinical experiences in OB/GYN, and a breadth of academic performance on stan-
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>GO FOR IT</th>
<th>Control</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>11</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Age (year)</td>
<td>26 (25,27)</td>
<td>26 (25,26)</td>
<td>.60</td>
</tr>
<tr>
<td>Year of medical school graduation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>10 (90.9)</td>
<td>18 (100)</td>
<td>.38</td>
</tr>
<tr>
<td>Prior to 2013</td>
<td>1 (9.1)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>USMLE scores</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Step 1</td>
<td>222 (206,237)</td>
<td>223 (212,228)</td>
<td>.64</td>
</tr>
<tr>
<td>Step 2 clinical knowledge</td>
<td>246 (227,259)</td>
<td>238 (233,249)</td>
<td>.34</td>
</tr>
<tr>
<td>Step 2 clinical skills</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pass</td>
<td>11 (100)</td>
<td>17 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>Fail</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Time spent in OB/GYN clinical activities (weeks)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M3 Year</td>
<td>6 (6,8)</td>
<td>6 (6,9)</td>
<td>.66</td>
</tr>
<tr>
<td>M4 Year</td>
<td>4 (4,8)</td>
<td>8 (8,12)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Month of final OB/GYN clinical experience</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jul-Sep 2012</td>
<td>5 (45.4)</td>
<td>4 (22.2)</td>
<td>.31</td>
</tr>
<tr>
<td>Oct-Nov 2012</td>
<td>3 (27.3)</td>
<td>10 (55.6)</td>
<td></td>
</tr>
<tr>
<td>Jan-May 2013</td>
<td>3 (27.3)</td>
<td>4 (22.2)</td>
<td></td>
</tr>
<tr>
<td>Month of final M4 clinical experience</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan-Feb 2013</td>
<td>3 (27.3)</td>
<td>3 (16.7)</td>
<td>.23</td>
</tr>
<tr>
<td>Mar 2013</td>
<td>6 (54.5)</td>
<td>6 (33.3)</td>
<td></td>
</tr>
<tr>
<td>Apr-May 2013</td>
<td>2 (18.2)</td>
<td>9 (50.0)</td>
<td></td>
</tr>
<tr>
<td>Self-rated baseline clinical skills/procedural competency*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comprehensive women’s health history</td>
<td>4 (3,4)</td>
<td>4 (3,4)</td>
<td>.68</td>
</tr>
<tr>
<td>Breast exam</td>
<td>4 (3,4)</td>
<td>4 (3,4)</td>
<td>.62</td>
</tr>
<tr>
<td>Pelvic exam</td>
<td>3 (3,4)</td>
<td>3 (3,4)</td>
<td>.20</td>
</tr>
<tr>
<td>Two-handed knot-tying</td>
<td>3 (2,3)</td>
<td>3 (3,4)</td>
<td>.01</td>
</tr>
<tr>
<td>Intrapartum cervical assessment</td>
<td>2 (2,3)</td>
<td>2 (2,3)</td>
<td>.34</td>
</tr>
<tr>
<td>Normal vaginal delivery</td>
<td>2 (2,2)</td>
<td>2.5 (2,3)</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>2nd-degree vaginal laceration repair</td>
<td>1 (1,2)</td>
<td>2 (1,2)</td>
<td>.36</td>
</tr>
<tr>
<td>Electronic fetal heart rate interpretation</td>
<td>2.5 (2,3)</td>
<td>3 (3,3)</td>
<td>.26</td>
</tr>
<tr>
<td>Intrauterine device insertion</td>
<td>2 (2,3)</td>
<td>2 (1,2)</td>
<td>.96</td>
</tr>
<tr>
<td>Endometrial biopsy</td>
<td>2 (0,2)</td>
<td>2 (1,2)</td>
<td>.44</td>
</tr>
<tr>
<td>Vaginal wet-prep interpretation</td>
<td>3 (2,4)</td>
<td>3 (3,4)</td>
<td>.24</td>
</tr>
</tbody>
</table>

All data reported as either frequency (percent) or median (25th, 75th percentile).*Median scores based on a 4-point Likert-type scale with scale anchors and values as follows: 1 = I am unable to perform the entire procedure under supervision; 2 = I am able to perform the procedure under supervision; 3 = I usually do not require supervision but maybe need help occasionally; 4 = I am competent to perform the procedure unsupervised (I can deal with complications).
standardized assessments (Table 3). Second, the 32 participants, representing 2.5% of the total number of students matching into OB/GYN in 2013, provided ample power for identifying statistically significant differences between groups. Finally, the inclusion of multiple forms of objective competency assessments strengthens the validity and generalizability of the findings.

Conversely, limitations of this study should be noted. First, we were unable to utilize a randomized study design due to recruitment limitations. The quasi-experimental educational study design is analogous to a prospective cohort clinical study design, with the same concerns regarding unequal distribution of confounders between groups. The similarity in the baseline character-

| Table 4: End-of-study clinical skills/procedural skills/knowledge competency outcomes. |
|------------------------------------------|-----------------|-----------------|-----------------|
|                                        | GO FOR IT        | Control         | P Value         |
| N                                       | 11              | 21              |                 |
| Composite outcome score                 | 73 (68,77)      | 41 (35,45)      | <.001           |
| Clinical skills OSCE¹                   |                 |                 |                 |
| Comprehensive women's health history (49 tasks) | 76 (69,86)      | 63 (53,69)      | <.01            |
| Breast/Pelvic physical exam (37 tasks)  | 78 (70,86)      | 62 (54,68)      | <.01            |
| Technical skills stations²              |                 |                 |                 |
| Two-handed square knot (%)              | 11 (100)        | 21 (100)        | 1.0             |
| Intrapartum cervical assessment         |                 |                 |                 |
| Dilation (5 tasks)                      | 60 (40,60)      | 20 (20,20)      | <.01            |
| Effacement (5 tasks)                    | 60 (60,80)      | 20 (10,40)      | <.01            |
| Composite of dilation & effacement (10 tasks) | 60 (50,70)      | 30 (20,30)      | <.01            |
| Normal vaginal delivery (23 tasks)      | 65 (52,78)      | 35 (26,48)      | <.01            |
| 2nd-degree vaginal laceration repair (12 tasks) | 92 (83,100)    | 50 (42,58)      | <.01            |
| IUD insertion (12 tasks)                | 67 (50,75)      | 33 (33,50)      | <.01            |
| Endometrial biopsy (7 tasks)            | 57 (43,71)      | 57 (43,71)      | .66             |
| Medical/Technical knowledge assessments  |                 |                 |                 |
| NBME Obstetrics & Gynecology Subject Exam³ | 58 (40,89)      | 49 (29,75)      | .41             |
| Surgical instrument identification      |                 |                 |                 |
| Name (31 tasks)                         | 87 (77,97)      | 26 (16,29)      | <.01            |
| Primary function (31 tasks)             | 61 (55,71)      | 32 (23,39)      | <.01            |
| Composite of name and function (62 tasks) | 74 (66,79)      | 29 (23,32)      | <.01            |
| Suture identification (7 tasks)         | 57 (43,71)      | 29 (14,43)      | <.01            |
| Surgical blade identification (3 tasks)  | 100 (33,100)    | 33 (0,50)       | <.01            |
| Surgical needle identification (8 tasks) | 75 (62,75)      | 0 (0,0)         | <.01            |

¹ Objective Structured Clinical Exam (OSCE) results reported as median percentage of checklist items (ie, tasks) rated as “well done.”
² Technical skill procedural checklist results reported as median percentage of checklist items (ie, tasks) rated as “complete” for each subject.
³ National Board of Medical Examiners (NBME) results reported as median overall-year percentiles for each subject.
Abbreviations and Acronyms
M4 = fourth year of medical school; OB/GYN = obstetrics and gynecology; GO FOR IT = Gynecology and Obstetrics Fundamentals of Residency Internship Training; ACGME = Accreditation Council for Graduate Medical Education; PSC = primary study center; DCC = Data Coordination Center; PI = principal investigator; PRIMER = Procedural Repetition Involving Montessori-type Experience and Rehearsal; NBME = National Board of Medical Examiners; OSCE = Objective Structured Clinical Exam

Correspondence
Address to:
Francis S. Nuthalapaty, MD, Greenville Health System, Department of OB/GYN, 890 W Faris Rd, Suite 470, Greenville, SC 29605 (fnuthalapaty@ghs.org)

112

Conclusion
The results of this study suggest that OB/GYN educators should implement intensive residency preparation courses near the end of the M4 year to prepare students to enter residency with appropriate skills and knowledge. The curriculum developed for the GO FOR IT Trial is now an integral component of the M4 curriculum at the University of South Carolina School of Medicine Greenville.

References
Blood Loss and Transfusions After Pericardial Closure Using a Porcine-Derived Extracellular Matrix

Timothy G. Johnson, MD; William W. Hope, MD; Howard F. Marks; and Peter N. Kane, MD

From the Department of General Surgery, New Hanover Regional Medical Center, Wilmington, NC (T.G.J., W.W.H.), and Department of Cardiothoracic Surgery, New Hanover Regional Medical Center, Wilmington, NC (H.F.M., P.N.K.)

Abstract

Background: At the onset of an open heart surgical procedure, the pericardium is opened to facilitate access to the heart and great vessels and was historically left open at the conclusion of the case to theoretically prevent iatrogenic cardiac tamponade. Studies from the 1970s showed that closing the pericardium was safe and potentially beneficial during repeat mediastinal entry. We evaluated the effect of closing the pericardium with a porcine-derived extracellular matrix (ECM) patch on postoperative blood loss and blood transfusion requirements.

Methods: We retrospectively reviewed consecutive open heart procedures by a single surgeon at a single center over 18 months who closed with patch closure of the pericardium or closed primarily. Mediastinal and chest tube outputs were used as surrogates for postoperative blood loss. Perioperative blood transfusions were tracked.

Results: We found no significant difference in postoperative blood loss from the mediastinal and chest tubes ($P > .05$), no difference in the timing of mediastinal and chest tube removal, and no difference in need for urgent reoperations between the 2 groups. We identified a statistically significant difference in postoperative blood transfusion requirements. Patients with patch closure of the pericardium required fewer transfusions per patient than patients with their pericardium closed primarily ($P = .0002$).

Conclusions: Closing the pericardium with CorMatrix ECM did not decrease the amount of postoperative blood loss but resulted in fewer blood transfusions per patient. Limitations to this study included a selection bias that favored the use of patch closure for younger patients, potentially confounding our results.
Methods
Following Institutional Review Board approval, we retrospectively reviewed consecutive open heart surgery cases from June 1, 2012, through December 21, 2013, performed by a single surgeon at our medical center. Data were obtained from our electronic medical records and from a prospectively collected database. Exclusion criteria included intra- and perioperative deaths and patients who left the operating room on ECMO (extracorporeal membrane oxygenation). The decision to use the extracellular matrix for closure of the pericardium was left to the discretion of the primary surgeon.

Primary endpoints were postoperative blood loss and postoperative blood transfusions in units of packed red blood cells transfused. Amount of chest tube and mediastinal tube output was used as a surrogate for postoperative blood loss. Secondary endpoints included date of mediastinal and chest tube removal and number of re-explorations. Basic demographic data included age and gender of the patients. Descriptive statistics were generated using t-test, Fisher's exact, and Χ² test of independence, with a P < .05 considered significant.

Results
During the 18-month study, 316 open heart procedures were performed. Eleven patients were excluded due to 4 patient deaths and 7 patients on ECMO. Of the 305 patients remaining in the study, 143 had their pericardium closed with CorMatrix ECM, and 162 patients had their pericardium closed primarily. There was no difference in patient gender between the 2 groups, but the closed pericardium group was significantly younger than the group primarily closed (Table 1).

Fluid output was recorded until the tube was removed or through postoperative day 3, and total perioperative tube output was compared. There was no significant difference in chest tube, mediastinal tube, and total tube output between the 2 groups (Fig. 1).

There was no significant difference between groups with regard to the timing of chest tube and mediastinal tube removal (Fig. 2) or in the rate or re-exploration for bleeding between the 2 groups (P > .05).

We found a statistically significant difference in units of blood transfused between the patch closed and the primarily closed groups (0.4 units vs. 0.9 units, P < .05) (Fig. 3).

Discussion
Closure of the pericardium at the conclusion of open heart surgery has been proven to be safe and effective, causing little ill effects on hemodynamics while minimizing postoperative adhesions to the posterior sternum.1-8 The primary advantage of closing the pericardium is decreased adhesions encountered during repeat median sternotomy. Though the rate of repeat median sternotomy has increased in the past due to willingness to perform cardiac revascularization on older patients,9-11 improved long-term patency of bypass grafts with vein and left internal mammary artery is extending the time between the first and subsequent cardiac revascularization procedures, causing a plateau in this rate.11 Subsequently, most patients who undergo a median sternotomy do not benefit from the primary advantage of a postoperative closed pericardium.

In our practice, we routinely try to close the pericardium if possible. In cases where pericardial closure may not be feasible due to pericardial contrac-

Table 1
Patient demographics in patch closed and primary closure groups.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patch Closed</th>
<th>Primary Closure</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>143</td>
<td>162</td>
<td></td>
</tr>
<tr>
<td>Gender, no. (%)</td>
<td></td>
<td></td>
<td>0.1273</td>
</tr>
<tr>
<td>Female</td>
<td>33 (23.1)</td>
<td>50 (30.9)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>110 (76.9)</td>
<td>112 (69.1)</td>
<td></td>
</tr>
<tr>
<td>Age, years (mean ± SD)</td>
<td>60.0 ± 9.1</td>
<td>69.9 ± 11.7</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Figure 1
Chest tube (CT), mediastinal tube (Medi), and total outputs were not significantly different between the study groups (P = .0631, P = .7654, and P = .1594).

Output Volume (cc)

<table>
<thead>
<tr>
<th></th>
<th>CT Output</th>
<th>Medi Output</th>
<th>Total Output</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patch Closed</td>
<td>Primary Closure</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>200</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>400</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>600</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>800</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1200</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1400</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1600</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
tion, cardiac enlargement, and lack of conduit in re-do operations, alternative means of closure are now available. There are several options to assist in pericardial closure, including autogenous tissue, such as a rotational pericardial flap or a pericardial fat pad, and synthetic or biosynthetic pericardial substitutes.

These substitutes include PTFE (polytetrafluoroethylene, GORE-TEX® [W. L. Gore & Associates, Inc., Flagstaff, Ariz, USA]), glutaraldehyde-treated xenografts, bioresorbable polymer films such as a barrier film containing polyactic acid and polyethylene glycol (REPEL-CV®, Sythemed Inc., Iselin, NJ, USA), and decellularized extracellular matrix such as CorMatrix ECM. CorMatrix ECM is produced from porcine small intestinal submucosa that is decellularized, leaving the complex extracellular matrix intact. CorMatrix ECM supports tissue repair, remodeling into functional pericardial tissue, and avoiding premature breakdown and calcification when used to close the pericardium. An explanted CorMatrix ECM patch used for a pericardial closure that was removed 5 years after the procedure showed that it had been almost fully recellularized, well integrated, and densely vascularized, similar to differentiated connective tissue.

Overall, there is a paucity of data examining the potential benefits of closing the pericardium with CorMatrix ECM. However, CorMatrix ECM has been shown to decrease the rate of postoperative atrial fibrillation in one retrospective study, though no randomized trial exists. Our report evaluates the use of CorMatrix ECM to close the pericardium, specifically evaluating whether we could find a secondary benefit beyond decreased reoperative adhesions to potentially offset the cost of the product used to close the pericardium. We focused our attention on blood loss and transfusion requirements, knowing that blood transfusion after cardiac surgery is a risk factor for increased length of stay if more than 3 units of blood were transfused and shorter length of stay could potentially offset the material cost of the patch.

We successfully showed a decreased transfusion need in patients who underwent patch closure of their pericardium, but likely not enough to offset the cost or affect length of stay. This decrease in transfusion requirement is difficult to explain as the blood loss and chest tube outputs were not different. One explanation is that although our cardiovascular intensive care unit and program, like many, has protocols and triggers for blood transfusion based on hemoglobin/hematocrit levels, there is also some subjectivity. In our unit, blood transfusions are based on certain triggers but also...
depend on the hemodynamic and overall clinical picture of the patient; as a result, variability can arise, which likely explains the significant difference that likely has no major clinical bearing. Determining the clinical significance of this variability requires further study.

There are several limitations of our study inherent in a retrospective review. There was a significant difference in the group undergoing closure using the extracellular matrix compared with the group primarily closed, which could have altered the results. This is likely from surgeon bias and using this technique preferentially in younger patients, as the likelihood for reoperation is potentially higher due to a presumed longer life span. Furthermore, the decision about how to close the pericardium was made by the surgeon at the completion of the case based on many factors, introducing another selection bias.

We also did not evaluate the long-term outcomes of these patients or whether any had undergone reoperation. Previous literature, however, has supported decreased adhesions with closure of the pericardium even with pericardial substitutes.1,3,13,14,16

There was no difference in re-expansion requirements, which can be considered a corollary finding to the studies that showed no major hemodynamic differences between groups as previously mentioned. We also found no difference in the amount of chest and mediastinal tube output, as well as the time to removal of each tube. At the onset of our study, we hypothesized that compartmentalization of the mediastinum created by closing the pericardium may lead to less blood loss, either by physiologically tolerated compression not causing tamponade, or perhaps prevention of cytokines released from the fresh operative field contacting the cardiac tissue and causing coagulopathy.

Conclusion

In conclusion, the use of a porcine-derived extracellular matrix patch to close the pericardium after open heart surgery resulted in no significant differences in chest tube output or time to removal of tubes or the reoperative rate for bleeding compared with primary closure. There was a significant difference in transfusion requirements in the CorMatrix ECM pericardial closure group, although this difference is likely not clinically significant and requires further study. Future randomized studies using pericardial closure techniques are needed to determine the true benefits of this procedure. Furthermore, a thorough analysis of risk factors that places a patient at increased risk of requiring a repeat median sternotomy may allow cardiothoracic surgeons to selectively close the pericardium of these patients.

References

Impact of Methicillin-Resistant Staphylococcus aureus (MRSA) Decolonization Protocol on Colonization and Infection Rates in a Level III Neonatal Intensive Care Unit

Myah Griffin, MD; Nirav T. Patil, MBBS, MPH; and Robin N. LaCroix, MD

From the University of South Carolina School of Medicine Greenville, Greenville, SC (M.G.); Department of Quality Management, Greenville Health System, Greenville, SC (N.T.P.); and Department of Pediatrics, Division of Pediatric Infectious Disease, Greenville Health System, Greenville, SC (R.N.L.)

Abstract

**Background:** In recent decades, the US has seen a substantial increase in Methicillin-resistant Staphylococcus aureus (MRSA) infections and outbreaks in neonatal intensive care units (NICU). In an effort to eliminate MRSA infections and potential outbreaks, in 2005 we implemented a MRSA Decolonization Protocol in our Level III NICU. The protocol primarily consisted of 4 pieces: 1) contact precautions, 2) Hibiclens® bath, 3) mupirocin ointment to the nares, and 4) continued surface surveillance cultures. The purpose of this 10-year study was to determine the impact our NICU Decolonization Protocol had on the rates of MRSA colonization and infection.

**Methods:** All neonates born between January 2002 and December 2012 (N = 8283) admitted to our Level III NICU were identified. Patients were subsequently divided into 2 groups based on date of protocol implementation: Group 1 consisted of neonates born preprotocol (January 2002–December 2004) and Group 2 of neonates born postprotocol (January 2005–December 2012). Frequency of MRSA colonization and infection were our primary endpoints.

**Results:** Group 1 included 2139 infants, of whom 96 developed MRSA colonization (n = 87) and/or infection (n = 9). Group 2 had 6144 infants; 178 developed MRSA colonization (n = 167) and/or infection (n = 11). The frequency of MRSA colonization (Group 1: 4.1% vs. Group 2: 2.7%; \( P = .002 \)) and infection (0.4% vs. 0.2%; \( P = .05 \)) was significantly lower in Group 2.

**Conclusions:** The proportion of neonates with MRSA colonization and/or infection in our Level III NICU was significantly reduced following implementation of a decolonization protocol.

**Methodology:**

Methicillin-resistant Staphylococcus aureus (MRSA) is a common bacterium that has become endemic to hospitals. Infants in neonatal intensive care units (NICU) represent a particularly at-risk population. Factors such as young gestational age, low birth weight, need for surgical procedures, and utilization of devices, such as mechanical ventilation, have been shown to predispose infants to MRSA colonization and infection. A large number of humans (30%–70%) are carriers of Staphylococcus aureus. Neonates are often exposed shortly following birth via the environment and/or their parent’s or healthcare worker’s skin. Between 1995 and 2004, NICUs in the US experienced a 300% increase in MRSA infections. Around 2001 and 2002, we also noticed an amplified rate of MRSA colonization and infection.

In an effort to eliminate subsequent infections and potential MRSA outbreaks, we implemented a MRSA Decolonization Protocol in our Level III NICU. This protocol was first applied in January 2005 and primarily consisted of 4 pieces: 1) contact precautions, 2) Hibiclens® bath, 3) mupirocin ointment to the nares, and 4) continued surface surveillance cultures. Hand hygiene is also an
area of emphasis, as staff members are required to perform hand hygiene before and after caring for and/or handling infants. In addition, both staff and parents are required to wear gloves and gowns while in the patient’s room if they have a positive culture for MRSA.

MRSA infection is associated with significant morbidity in infants, as it can result in subsequent infections; these include, but are not limited to, skin infections, conjunctivitis, blood stream infections, surgical site infections, pneumonia, meningitis, and respiratory tract infections. NICUs throughout the country have sought to reduce MRSA infections and outbreaks; however, as of 2005, optimal management strategies remained unclear. The purpose of this study was to determine the impact of a NICU MRSA Decolonization Protocol on neonatal rates of MRSA colonization and infection.

**Methods**

Following approval from the Greenville Health System Institutional Review Board, we identified all neonates born between January 2002 and December 2012 (N = 8283) admitted to the Level III NICU at Greenville Memorial Medical Center (GMMC), a large, tertiary care academic health center. These patients were subsequently divided into 2 groups based on date of protocol implementation: Group 1 consisted of neonates born preprotocol (January 2001–December 2004) and Group 2 of neonates born postprotocol (January 2005–December 2012). Neonates colonized or infected with MRSA (n = 274) were then identified by retrospective chart review. Infants transferred from an outside institution or another floor at GMMC with a MRSA-positive culture upon admission were excluded from this study (n = 15).

Data collection included gender, birth weight, gestational age, mode of delivery, placement of PICC (peripherally inserted central catheter) line, presence of necrotizing enterocolitis (NEC) or other infections, surgery, and MRSA strain. Primary endpoints were incidence of MRSA colonization and infection. MRSA colonization was defined as having a MRSA-positive culture of the anterior nares and/or skin surface. MRSA infection was defined as having a MRSA-positive culture from blood, wound(s), tracheal aspirate, urine, or cerebrospinal fluid.

Surveillance cultures were collected 1–2 times per week on all infants in the NICU who were not under contact precautions for MRSA. Naso-pharyngeal, axillary, and perianal areas were swabbed with 3 individual cotton swabs and placed inside a single vial with sterile saline solution. During Group 1’s study period (prior to 2005), all vials were centrifuged and transferred to sheep blood plates in the GMMC laboratory; this process took between 4 and 5 days to produce a positive culture. Starting in 2005 (Group 2), the laboratory began using Chrome Agar® in place of sheep blood plates; this change enabled growth observation at approximately 24 hours. MRSA strains were further characterized using pulsed-field gel electrophoresis.

The MRSA Decolonization Protocol included a physician’s order for MRSA isolation, contact precautions, a Hibiclens bath, mupirocin (Bactroban®) to nares 2 times per day for 5 days, and continued surface surveillance cultures until Infection Prevention approved removal from isolation. Standard policy in the NICU required all staff members to follow contact precautions and to perform hand hygiene before and after caring for and/or handling infants. Additional measures required parents to wear gloves and gowns when in the room with their infant if they had a positive culture for MRSA.

Patients included in the analysis were not colonized or infected upon admission to the NICU. Bivariate analysis was performed to compare infant characteristics between study groups.

Categorical variables were compared using Chi-square test. Continuous variables were compared using student’s t-test. Data are presented as frequency and percentage for categorical variables or mean ± standard deviation for continuous variables. P values < .05 were considered indicative of statistical significance. All statistical analyses were completed using SAS Enterprise Guide 7.1 software (Statistical Analysis System, Cary, NC).

**Results**

During the study period, 8283 neonates were admitted to the NICU at GMMC and met the inclusion criteria. From these, 2139 were born preprotocol (Group 1), of whom 96 developed MRSA colonization (n = 87) and/or infection (n = 9). From the 6144 infants born postprotocol (Group 2), 178 developed MRSA colonization (n = 167) and/or infection (n = 11). All 20 patients who were infected with MRSA were infected prior to identification of colonization. The frequency of MRSA colonization (Group 1: 4.1% vs. Group 2: 2.7%; P = .002) was significantly lower in Group
IMPACT OF MRSA DECOLONIZATION PROTOCOL IN NICU

2; frequency of MRSA infection was also lower in Group 2, although only marginally significant (0.4% vs. 0.2%; \( P = .05 \)) (Table 1).

Patient demographics and risk factors are described in Table 2. Neonates born preprotocol and postprotocol were comparable with regard to gender, birth weight, gestational age, PICC line placement, mechanical ventilation, and days to colonization. Mode of delivery and need for surgery were significantly different between groups, with a higher proportion of neonates in Group 1 born by C-section (77.1% vs. 65.2%, \( P = .04 \)) and a higher proportion of infants in Group 2 requiring surgery (49.0% vs. 70.0%, \( P < .01 \)).

From the 274 colonized infants, 179 (65%) had strain typing data available. From these, 14 unrelated MRSA strains were identified, of which community-associated MRSA USA300 was most common (\( n = 28 \)), followed by hospital-associated MRSA USA800 (\( n = 22 \)). One MRSA infection progressed to sepsis and ultimately necrotizing pneumonia and resulted in death; this was the only mortality in the study. MRSA strain VIIc was the causative organism in this mortality—this was the only infant colonized with this particular strain.

Discussion

MRSA colonization is a risk factor for progression to infection.\(^2\) This study demonstrates that efforts to decolonize neonates can statistically impact rates of infection. This study is the first to describe the benefit of decolonization in a vulnerable group of infants. There were no adverse events associated with the use of the topical chlorhexidine and mupirocin.

Infections in neonates are associated with increased cost, prolonged length of stay, exposure to additional antibiotics, and increased invasive procedures such as central venous access, lumbar puncture, and even surgical interventions.\(^{12,13}\) Additionally, new literature reports invasive bloodstream infections lead to increased risk of poor neurodevelopmental outcomes in preterm infants.\(^{14,15}\)

Efforts to prevent colonization with MRSA should be first line. By using active surveillance to identify infants who become colonized early and adherence to expanded contact precautions that include family members, in addition to healthcare workers, the decrease in transmission of MRSA in the NICU setting can be accomplished. However, if colonization occurs, additional measures to decrease or eliminate bacterial bioburden appear to decrease the risk of progression to infection.

Conclusion

This study demonstrates that measures of active surveillance for early recognition of colonization and isolation combined with implementation of a NICU MRSA decolonization protocol can reduce colonization and infection rates, and the associated morbidities attributable to infection.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>MRSA status preprotocol and postprotocol.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preprotocol</td>
</tr>
<tr>
<td>N</td>
<td>2139</td>
</tr>
<tr>
<td>Infection, no. (%)</td>
<td>9 (0.42%)</td>
</tr>
<tr>
<td>Colonization, no. (%)</td>
<td>87 (4.07)</td>
</tr>
<tr>
<td>Total: infected or colonized, no. (%)</td>
<td>96 (4.49)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Patient demographics and risk factors.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preprotocol</td>
</tr>
<tr>
<td>N</td>
<td>96</td>
</tr>
<tr>
<td>Female, no. (%)</td>
<td>48 (50.0)</td>
</tr>
<tr>
<td>Pre-term delivery, no. (%)</td>
<td>92 (95.8)</td>
</tr>
<tr>
<td>Gestational age, no. (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;36 weeks</td>
<td>86 (89.6)</td>
</tr>
<tr>
<td>&lt;32 weeks</td>
<td>61 (63.5)</td>
</tr>
<tr>
<td>Mode of delivery, no. (%)</td>
<td></td>
</tr>
<tr>
<td>C-section</td>
<td>74 (77.1)</td>
</tr>
<tr>
<td>Birth weight (kg), mean ± SD</td>
<td>1.52 ± 0.88</td>
</tr>
<tr>
<td>Low birth weight (&lt;2.5kg)</td>
<td>83 (86.4)</td>
</tr>
<tr>
<td>Days to colonization, mean ± SD</td>
<td>20.4 ± 20.8</td>
</tr>
<tr>
<td>Mechanical ventilation, no. (%)</td>
<td>21 (21.9)</td>
</tr>
<tr>
<td>PICC line, no. (%)</td>
<td>66 (68.7)</td>
</tr>
<tr>
<td>Surgery, no. (%)</td>
<td>47 (49.0)</td>
</tr>
<tr>
<td>SD, standard deviation; PICC, peripherally inserted central catheter</td>
<td></td>
</tr>
</tbody>
</table>
References


Does Comprehensive Dementia Education Impact Self-Efficacy Among Family Caregivers in the Community?

Xi Pan, PhD; Melissa Bailey, DO, MPH; Meghan Socko, LMSW; and Lisa Naylor, NP

From the Department of Public Health Sciences, Clemson University, Clemson, SC (X.P.), and Division of Geriatrics, Center for Success in Aging, Greenville Health System, Greenville, SC (M.B., M.S., L.N.)

Abstract

Background: This pilot study assessed the impact of a 6-week comprehensive, multisession, professionally guided, and in-person caregiver educational program on self-efficacy among dementia family caregivers in Upstate South Carolina (SC).

Methods: Self-efficacy among 28 family dementia caregivers was analyzed using data collected in 2015 with repeated-measure of linear regression (ANOVA).

Results: Results show that caregiver self-efficacy in managing dementia symptoms and the utilization of social support services are significantly improved after the training.

Conclusions: Findings of the study imply that caregiver education is beneficial in reducing caregiver burnout and optimizing caregiver needs for dementia caregiving. This finding is helpful to develop family-centered interventions that should be considered as a part of routine dementia treatment protocol in Upstate SC.

Alzheimer’s disease and related dementia (ADRD) poses increasing challenges for public health and requires substantial resources for dementia care in the United States (US). In 2015, more than 15 million Americans provided unpaid care (informal care) to their loved ones with ADRD, and 85% of the caregivers were family members. Family caregivers are burdened with the complexity of providing assistance in basic and instrumental activities of daily living. Many caregivers lack dementia education and are unprepared for the demands that the disease places on their time, resources, and health. Furthermore, compared to non-dementia caregivers, dementia caregivers tend to become more socially isolated from their peers and others in the community. The demands and emotional strains associated with dementia caregiving reduce caregivers’ physical and psychological well-being and leave them vulnerable to depression.

Self-efficacy plays a key role in the relationship between dementia caregiving and depression among caregivers. Self-efficacy refers to an individual’s belief/assessment of his or her ability to successfully perform daily management of dementia by learning specific behaviors or tasks relevant to the disease. Higher levels of self-efficacy predict higher capability of accomplishing dementia care management and enduring the disease-related challenges, whereas lower levels of self-efficacy predict higher levels of stress and depression. Social support and resources are important for providing emotional support to caregivers and enhancing their self-efficacy, which can encourage them to access information and education that may aid in the caregiving journey. The majority of existing dementia education programs in the US are offered online, emphasize dementia symptom management without fostering the benefits of social support, and are not facilitated by healthcare professionals. Many of these programs are challenging for dementia caregivers, particularly older caregivers, who have limited or no access to the internet and are not computer savvy. What appears to be lacking is the availability of face-to-face, comprehensive educational programs that focus on multiple aspects of dementia—from basic education to the challenges that may arise in the
The caregiving process, including safety concerns and expectations at each stage of the disease process. Empirically derived interventions that match the needs and preferences of caregivers in specific communities are underdeveloped. Existing literature on interventions that effectively improve key outcomes for family caregivers is limited.

The objective of this study was to evaluate Caregiver ABCs program, a comprehensive caregiver education, created by the Center for Success in Aging at Greenville Health System (GHS) in Greenville, South Carolina (SC). The focus of the study was assessment of self-efficacy among the family caregivers in Upstate SC (Greenville-Spartanburg-Anderson) participating in the Caregiver ABCs program. It was hypothesized that the comprehensive education would have a positive effect on family caregiver self-efficacy in managing dementia symptoms and increase caregiver use of social support resources.

Methods

Intervention

The Caregiver ABCs program is a 6-week comprehensive educational series consisting of 6 classes: 1) Alzheimer’s, Aging, and Assessment, 2) Behaviors, Beliefs, and the Baggage We Bring, 3) Communication, Caring, and Coping, 4) Driving, Dangers, and Drugs, 5) Elder Law, and 6) Expectations, Emergencies, and Enjoyment. The aims of the program were to enhance the caregivers’ knowledge in dementia caregiving and to learn to reduce caregiver stress. Each class lasts 120 minutes and is taught by nurse practitioners and a licensed social worker, who regularly provide health care to individuals with ADRD in an outpatient setting at GHS. The class series is repeated 3 times annually.

Sample

Our study population included family caregivers of people with diagnoses of ADRD who registered for the Caregiver ABCs program between January 2015 and October 2015 from Upstate SC. The total number of registrants for each series was 30 (90 for all 3 series). Fifty-five registrants, including non-family caregivers (85%) and family caregivers who decided not to participate in the study (15%) as well as 7 people who missed the post-tests, were excluded from the analysis. Finally, the sample of the study consisted of 28 family caregivers who attended all 6 classes and completed the pre- and post-tests. This study was approved by the GHS Institutional Review Board before the start date of the first series in January 2015.

Measurement

Self-efficacy was measured using 10 items from the self-reported self-efficacy survey for dementia caregivers. Each item had 10 response categories scoring from 1 (Not at all) to 10 (Very certain). The first 5 items measured caregivers’ self-efficacy in managing dementia symptoms; the remaining 5 items measured use of social support services (Table 2, right). Validity (internal consistency) and reliability of the measurement were high with Cronbach’s alpha = .77 and .78, respectively.

Characteristics of participants, including chronological age, gender, race, education, marital status, relationship to care recipients, and living arrange-

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean ± SD)</td>
<td>62 ± 6</td>
</tr>
<tr>
<td>Gender, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>21 (75.0)</td>
</tr>
<tr>
<td>Race, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>27 (96.4)</td>
</tr>
<tr>
<td>African American</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Education, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Less than 8th grade</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Some high school</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>High school graduate</td>
<td>3 (10.7)</td>
</tr>
<tr>
<td>Some college</td>
<td>9 (32.1)</td>
</tr>
<tr>
<td>College graduate</td>
<td>14 (50.0)</td>
</tr>
<tr>
<td>Graduate school</td>
<td>2 (7.1)</td>
</tr>
<tr>
<td>Marital status, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Single or never married</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Married</td>
<td>23 (82.1)</td>
</tr>
<tr>
<td>Living with a partner</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Divorced or separated</td>
<td>3 (10.7)</td>
</tr>
<tr>
<td>Widowed</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Relationship to care recipients, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Spouse or partner</td>
<td>5 (17.9)</td>
</tr>
<tr>
<td>Adult child</td>
<td>19 (67.9)</td>
</tr>
<tr>
<td>Other family member</td>
<td>4 (14.2)</td>
</tr>
<tr>
<td>Friend</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Living with care recipients, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14 (50.0)</td>
</tr>
</tbody>
</table>
ment with care recipients, were collected. Education was defined as the highest level of degree that the family caregiver had received. Living arrangements were defined as whether the family caregiver was living with the care recipient by the time of study. In addition, self-rated health was a confounder and measured by a global question on caregivers’ general health status with 5-Likert scale response categories from “Poor” to “Excellent.”

Analysis
Descriptive statistics (eg, mean ± standard deviation and percentage) were used to examine characteristics of participants. Cohen's $d$ analysis was used to estimate effect size. Repeated-measure of linear regression (ANOVA) with a Greenhouse-Geisser correction was used to examine the changes in the mean of self-efficacy before and after the program. Post hoc tests using the Bonferroni correction was used to decide how much the mean of self-efficacy changed before and after the training. All analyses were conducted using IBM® SPSS® Statistics 23.0.

Results
Participant characteristics are described in Table 1 (left). Most of the 28 caregivers were Caucasian (96.4%) women (75.0%) with a mean age of 62 ± 6 years. Most were married (82.1%) and had earned college degrees (57.1%). Most of the caregiver participants were adult children (67.9%) and were living with the care recipients (50.0%) by the time of study. All participants in our study scored their self-rated health as Good/Very good (78.6%) or Excellent (21.4%) (Table 1).

Figure 1
Difference in caregiver self-efficacy scores pre-training and post-training.

Mean Total Scores of Self-Efficacy

<table>
<thead>
<tr>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; .001</td>
</tr>
</tbody>
</table>

Table 2
Effect of dementia education on caregiver self-efficacy (pre-post) ANOVA test.

<table>
<thead>
<tr>
<th>Self-Efficacy Items</th>
<th>Pre-training Score (mean ± SD)</th>
<th>Post-training Score (mean ± SD)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia symptom management (overall)</td>
<td>26.7 ± 10.8</td>
<td>40.3 ± 5.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>1 Handle any problems like memory loss</td>
<td>5.5 ± 2.9</td>
<td>7.9 ± 1.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2 Deal with frustration of caring</td>
<td>4.4 ± 2.7</td>
<td>8.0 ± 1.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>3 Handle problems that come up in future</td>
<td>5.2 ± 2.4</td>
<td>7.5 ± 1.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>4 Do something to keep relative independent</td>
<td>5.7 ± 2.8</td>
<td>8.2 ± 1.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>5 Care for relative without help from organizations or agencies</td>
<td>5.9 ± 2.0</td>
<td>8.7 ± 1.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Finding social support (overall)</td>
<td>24.6 ± 9.5</td>
<td>37.1 ± 7.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>6 Find ways to pay for services</td>
<td>4.1 ± 2.7</td>
<td>5.6 ± 2.8</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>7 Get answers to all questions about services</td>
<td>5.5 ± 2.5</td>
<td>8.5 ± 1.6</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>8 Find organizations or agencies that provide services</td>
<td>5.5 ± 2.3</td>
<td>8.5 ± 1.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>9 Arrange for services yourself</td>
<td>4.7 ± 2.4</td>
<td>7.7 ± 1.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>10 Get answers to all your questions about your relative’s care</td>
<td>4.8 ± 2.9</td>
<td>6.9 ± 2.2</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Note: Each item had 10 response categories scoring from 1 (Not at all) to 10 (Very certain). The first 5 items measured caregivers’ self-efficacy in managing dementia symptoms, and the remaining 5 items measured the use of social support services (max overall score = 50).
The mean scores of self-efficacy before and after the training were significantly different based on the ANOVA test (Fig. 1 and Table 2). As shown in Table 2, the mean post-training score of self-efficacy in managing dementia symptoms was significantly higher than that of pre-training (40.3 vs. 26.7; \( P < .001 \)). An increase was also seen with regard to self-efficacy in finding social support services among caregivers who participated in the program (24.6 vs. 37.1; \( P < .001 \)).

**Discussion**

Findings of this study suggest that this comprehensive, multisession, professionally guided, and in-person program was beneficial in providing significant knowledge, skills, and confidence to family caregivers. Caregivers also learned to address disease-related safety issues such as driving, cooking, and other activities that may require supervision. Therefore, the effectiveness of training of such brevity suggests that this intervention should be developed into a protocol and implemented as a part of routine clinical care in Upstate SC.

This study also supports the family-centered program of dementia care. Caregiving has a strong impact on family relationships and might determine the level of conflict within the family.\(^\text{12}\) The class of “Communication, Caring, and Coping” helps primary caregivers clarify expectations of caregiving among family members, identify potential sources of support, and address conflict resolutions. Positive and supportive family relationships have been found to be significantly associated with less strain and burden among caregivers, compared to caregivers with poor family functioning.\(^\text{12}\) The Caregiver ABCs program achieved the goal of increasing caregiver confidence in multifaceted dementia care, which helps health providers develop family-centered comprehensive dementia care for caregivers in other similar community settings.

Study limitations include small sample size, lack of control group, and inability to collect information on the severity of dementia among care recipients. Our sample also lacks diversity since the participants were mainly Caucasian married women with higher education. However, existing literature has suggested that caregivers who participate in psychoeducation tend to be female Caucasians with higher education.\(^\text{13}\)

To have a greater population health impact and to reach a greater percentage of the 45 million Americans and families affected by dementia and related diseases, expanding our study to include a more diverse cohort of participants at multiple sites is our future direction. As telehealth strategies are becoming increasingly popular, an online or computer-based psychoeducation model will be a promising supplement to our existing in-person sessions.

A big strength of internet-based psychoeducation is the removal of some barriers, such as the inability to leave the care recipient to attend a program.\(^\text{14}\) Existing evidence has shown that computer-based psychoeducation can improve caregiving confidence or mastery (ie, self-efficacy) among dementia caregivers.\(^\text{14,15}\) It is possible that an online program might accomplish similar outcomes among dementia caregivers in Upstate SC. Such a program can be provided to caregivers who have difficulty leaving the care recipient to attend in-person sessions. Thus, the combination of both programs may increase the recruitment, enhance participant diversity, and improve the interactivity between instructors and participants.

In addition, we plan to expand the follow-up investigation with longer intervals and to include a comparison group. It is unclear if this intervention would have been as effective in those with lower education or those less likely to take advantage of this type of program.

A comparison group with people who have lower education will be included in future studies. It is important to examine the influence of educational level on the relationship between self-efficacy and the intervention. Furthermore, qualitative studies such as interview or focus group are needed to understand why participants drop out from the program or decline to participate. Increased marketing and cultural sensitivity are also areas that we plan to expand. Last, correlating the stage of dementia with the pre- and post-training sessions will provide even more strength to our novel intervention.
DEMENTIA EDUCATION, SELF-EFFICACY, FAMILY CAREGIVERS

References


There is a large and increasing demand for organ transplantation. In the United States (US), approximately 9000 people donate organs each year, but more than 120,000 people are in need of a lifesaving organ transplant. According to the United Network for Organ Sharing (UNOS), organs are matched with transplant candidates using medical and logistical factors alone, with social characteristics, including insurance coverage, playing no role in transplant priority. However, to be matched, the patient must first be added to the national waiting list, an action determined by a hospital's transplant team.

Organs are a scarce resource, and the long-term viability of transplanted organs is a major concern for transplant centers, as failure can negatively impact their program's percentile of successful transplants. Transplantation is also expensive, ranging from about $334,000 for a kidney to over $1.2 million for a heart transplant. Moreover, these initial costs do not include the necessary antirejection drugs past 180 days, the cost of which can exceed $2500 per month. As a result, patients are unlikely to be placed on the transplant waiting list if they are uninsured, underinsured, and/or lack sufficient financial resources for the transplant surgery and the subsequent follow-up and antirejection medication required posttransplant.

In contrast, financial and insurance status are not considered necessary for organ donation. Due to this discrepancy, some critics believe the organ allocation system to be unequitable. Few studies,
INSURANCE STATUS OF DECEASED ORGAN DONORS

however, have examined this criticism. The aim of this study was to evaluate the insurance status of deceased organ transplant donors within a single Donor Service Area (DSA) to determine whether a disparity in insurance status exists between organ donors and organ recipients.

Methods
Rush University Medical Center’s Institutional Review Board approved this study. We performed a retrospective chart review from a prospective database on all patients whose organs were procured in Northern Illinois and Northwestern Indiana between January 2010 and December 2012 from the organ procurement organization (OPO), Gift of Hope. Data collection included donor age, sex, race, citizenship, and insurance status. Data were evaluated using student’s t-test and Fisher’s exact test. Statistical significance was assessed using alpha = .05. All data analysis was generated using SAS software, Version 9.1.3 (Statistical Analysis System, Cary, NC).

Results
During the study time frame, 816 organ transplant donors were identified and evaluated for transplant purposes. Donor characteristics are described in Table 1. The majority of patients were men (59%) and either Caucasian (59%) or African American (27%). The median donor age was 45 years, with a range of 1 month to 85 years. Donor insurance status was not attainable in 128 patients (16%). From donors in whom insurance status was available (n = 688), 70.5% (485) were insured and 29.5% (203) had no insurance (Table 2). African American (P = .017) and Latino (P < .0001) organ donors were less likely to have insurance when compared to their Caucasian counterparts. Approximately 3.5% (n = 24) of donors were non-US citizens, all of whom were uninsured.

Discussion
In 2008, Herring et al reported a story of a young, previously healthy, uninsured day laborer who presented to an emergency department in need of a heart transplant. The patient was ultimately deemed unsuitable, as he did not have the ability to pay for the long-term immunosuppressive therapy required for successful recovery; the patient died 2 weeks later. This experience acted as an impetus for the Herring et al study, which

---

### Table 1
Transplant donor characteristics.

<table>
<thead>
<tr>
<th>Patients, N</th>
<th>816</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median</td>
<td>45</td>
</tr>
<tr>
<td>Gender, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>482 (59.1)</td>
</tr>
<tr>
<td>Female</td>
<td>334 (40.9)</td>
</tr>
<tr>
<td>Race, no. (%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>481 (58.9)</td>
</tr>
<tr>
<td>African American</td>
<td>218 (26.7)</td>
</tr>
<tr>
<td>Latino</td>
<td>94</td>
</tr>
<tr>
<td>Asian</td>
<td>14  (1.8)</td>
</tr>
<tr>
<td>Other</td>
<td>9   (1.1)</td>
</tr>
<tr>
<td>Non-US citizens, no. (%)</td>
<td>24 (3.5)</td>
</tr>
</tbody>
</table>

### Table 2
Transplant donor ethnicity and insurance status.

<table>
<thead>
<tr>
<th>Patients, N</th>
<th>816</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian, no.</td>
<td>481</td>
</tr>
<tr>
<td>Yes, no. (%)</td>
<td>315 (65.5)</td>
</tr>
<tr>
<td>No</td>
<td>98  (20.4)</td>
</tr>
<tr>
<td>Unknown</td>
<td>68  (14.1)</td>
</tr>
<tr>
<td>African American, no.</td>
<td>218</td>
</tr>
<tr>
<td>Yes, no. (%)</td>
<td>119 (54.6)</td>
</tr>
<tr>
<td>No</td>
<td>58  (26.6)</td>
</tr>
<tr>
<td>Unknown</td>
<td>41  (18.8)</td>
</tr>
<tr>
<td>Latino, no.</td>
<td>94</td>
</tr>
<tr>
<td>Yes, no. (%)</td>
<td>46 (48.9)</td>
</tr>
<tr>
<td>No</td>
<td>40  (42.6)</td>
</tr>
<tr>
<td>Unknown</td>
<td>8   (8.5)</td>
</tr>
<tr>
<td>Asian, no.</td>
<td>14</td>
</tr>
<tr>
<td>Yes, no. (%)</td>
<td>6  (42.9)</td>
</tr>
<tr>
<td>No</td>
<td>5   (35.7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3   (21.4)</td>
</tr>
<tr>
<td>Other, no.</td>
<td>9</td>
</tr>
<tr>
<td>Yes, no. (%)</td>
<td>3  (33.3)</td>
</tr>
<tr>
<td>No</td>
<td>5   (55.6)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1   (11.1)</td>
</tr>
</tbody>
</table>
analyzed the insurance status of US organ donors by using the 2003 National Inpatient Sample (NIS). Their study included 1447 organ donors and 4962 transplant recipients, from which 16.9% of organ donors were uninsured, compared to 0.8% of transplant recipients. Similar to our study, most organ donors in the NIS database were Caucasian (69.4%) and in their early 40s (mean age, 40.4 years). Their study, however, had slightly more female donors (56.1%), while ours reported more men (59.1%).

Our findings showed that 30% of deceased organ transplant donors were uninsured. There were, however, 128 donors with an unknown insurance status. If all of these 128 donors happened to be insured, the rate of uninsured donors at this single OPO would still be 25%. In 2005, King and colleagues queried the Siminoff’s National Study of Family Consent Donation database and found that approximately 23% of all organ donors are uninsured.7

Approximately 4% of patients in our study were non-US citizens. Between 1988 and 2007, 0.63% of organ transplants were received by patients of unknown citizenship; this same population, however, accounted for 2.5% of all organs donated.8

Another barrier to receiving an organ transplant is underinsurance. In 2012, more than 31 million Americans were defined as underinsured—an insured person who spends a high share of their income on medical care.9 Moreover, a report from the Department of Labor shows that only 45% of private industry health plans cover organ and tissue transplantation.10

The Patient Protection and Affordable Care Act (ACA) seeks to increase the number of insured patients in the US. However, it is unclear whether all insurance types provided under the ACA will cover transplantation. The ACA mandates coverage for basic primary care needs, but coverage for transplant care is not well understood. The ACA also explicitly prohibits undocumented immigrants in the US (12.5 million people) from participating on the healthcare exchanges or in Medicaid expansion.11 Future research is needed to determine the impact of the ACA on donor recipient rates.

The authors concede that the insurance status of transplant donors and transplant recipients is not entirely comparable. Transplant recipients often have chronic diseases that mandate expensive health care. These patients also typically have time to obtain insurance through government programs such as Medicare or Medicaid. In contrast, patients who are transplant donors often die suddenly and may not have chronic diseases that mandate expensive health care and need for insurance.

Proponents of the current organ allocation system may argue that many of these uninsured donors would be insurable if they themselves needed a transplant, and that the observed disparity in insurance status between donors and recipients is exaggerated. The distinction between “insurable uninsured” and “uninsurable uninsured,” however, is a theoretical argument with limited practical application. First, it is not possible to differentiate between these two groups at the time of organ donation. Furthermore, insurance status of the organ donor (living or deceased) is not taken into consideration when soliciting organs while it is almost universally mandated for organ recipients. Last, yes, an uninsured patient in need of a transplant may acquire federal insurance (Medicare or Medicaid) over time and then get placed on the waitlist; however, as illustrated by Herring et al, it is not uncommon for transplantable patients to die prior to receiving the insurance needed to be added to the waiting list.6

The authors also concede that long-term viability of transplanted organs is a major concern for transplant surgeons and transplant centers. The field of transplant surgery arguably has the highest level of regulation, making good outcomes almost mandatory. Transplant centers are reviewed by the Centers for Medicare & Medicaid Services (CMS) on the basis of their 1-year patient and organ survival rates. Ramifications for a low survival rate can include lengthy and expensive corrective processes, as well as the possibility of having to terminate the program.

Moreover, transplant surgeons often feel pressured to get the most good out of a very scarce resource. Transplant centers may argue that, because of the CMS and the pressure to deliver a very high success rate, their hands are tied and that patients with insurance are a safer and more strategic long-term choice. Some people in the transplant community do admit that disparities exist; however, it should be noted that many from the transplant community have also fought against certain utilitarian proposals—those proposing that organ priority be given to those most likely to live the longest instead of those next in line—in an effort to prevent further disparities.

Despite the intent of UNOS and the Organ Procurement and Transplantation Network to
promote equity in transplantation access, our findings show that a disparity in insurance status does exist between organ donors and organ recipients. Transplantation is profitable to pharmaceutical companies, organ procurement organizations, and hospitals. This profit is contingent upon organ donation from both insured and uninsured patients. This fact makes the equity concerns about access to transplantation for the uninsured even more acute.

This study has all of the inherent limitations of a retrospective study from a prospective database. This study was also limited in size and scope, as we only reviewed the insurance status of deceased organ donors from a single DSA and did not review the insurance status of living organ donors or donor recipients.

**Conclusion**

Society solicits organ donations from all of its members; however, there is a disparity between eligibility for organ donation versus eligibility for organ transplantation. Although insurance is mandatory to receive an organ transplant, this study demonstrates that many organ donors do not have health insurance.

**References**


Case Studies

Catastrophic Upper Gastrointestinal Bleed in Roux-en-Y Gastric Bypass Patients From Ulcer Erosion Into the Splenic Artery: Details of Rapid Surgical Management

Andrew J. Jones, BS, BA; Nathaniel Walsh, MD; Aaron Bolduc, MD; Sean Lee, MD; and Brian Lane, MD

From the Department of Surgery, Augusta University Health, Augusta, Ga (A.J.J., N.W., A.B., S.L., B.L.); Medical College of Georgia at Augusta University, Augusta, Ga (A.J.J., N.W., A.B., S.L., B.L.); and Department of Minimally Invasive and Digestive Diseases Surgery, Augusta University Health, Augusta, Ga (S.L., B.L.)

Abstract

Postoperative ulcer disease continues to be a long-term concern in patients who undergo Roux-en-Y gastric bypass (RYGB). This case series details the hospital courses and surgical interventions for 2 patients who survived catastrophic bleeding events from marginal ulcer and gastric pouch ulcer erosion into the proximal splenic artery. In both cases, endoscopic therapy failed and urgent surgical intervention was necessary due to patient instability. The Veith maneuver was employed in Patient A for supraceliac aortic control, and Patient B underwent a series of operations to repair the erosion and gastric pouch. The surgical approaches for management and a discussion of RYGB complications are included.

Postoperative ulcer disease continues to be a long-term concern in patients who undergo Roux-en-Y gastric bypass (RYGB). The true incidence of this complication is difficult to determine and varies depending on follow-up. Literature has described incidence ranging between 0.6% to 25%. Though the causes of marginal ulcers in these patients is often multifactorial, the most consistent risk factors appear to be recurrent use of nonsteroidal anti-inflammatory drugs, tobacco abuse, and Helicobacter pylori infection. Diabetes mellitus has also been described as a risk factor because of microangiopathic disease that predisposes the patient to ischemia and ulcer formation.

Patients often present with nonspecific symptoms such as epigastric pain, dysphagia, nausea, and vomiting. The majority of marginal ulcer disease cases are treated medically with proton pump inhibitors, sucralfate, and patient counseling. Medical management is successful in approximately 68% of patients.

In cases involving significant gastric pouch or marginal ulcer bleeding, standard endoscopic hemostatic techniques are the first line of therapy. Angiographic hemostasis techniques have also been utilized. We report 2 cases of RYGB patients who had catastrophic bleeding events from marginal ulcer and gastric pouch ulcer erosion into the proximal splenic artery where endoscopic therapy failed and urgent surgery was necessary due to patient instability.

Case Descriptions

Patient A

Patient A is a 52-year-old woman with metastatic cholangioadenocarcinoma on palliative chemotherapy who presented to our emergency department (ED) with sharp epigastric pain and bright red hematemesis for several hours. She had a past surgical history of RYGB. The malignancy was discovered incidentally following the RYGB 1 year before her presentation to our facility. She had developed chronic anemia, attributed to malignancy and/or chemotherapy, which was being treated with serial transfusions. The patient stated that she had chronic nausea since the discovery of her malignancy but very little vomiting prior to that day.
In the ED, she was tachycardic and mildly hypoten- sive. Her hemoglobin was 6.7 grams per deciliter, which was below her baseline of 8.0 grams per deciliter measured 3 days prior. She received 2 units of packed red blood cells (pRBC) and was admitted to the intensive care unit (ICU). Gastroenterology performed an esophagogastroduodenoscopy (EGD) that revealed bleeding from a marginal ulcer at the gastrojejunlal anastomosis.

Twenty-four hours later, the patient collapsed following an episode of frank hematemesis in the restroom. A code blue was called and the patient was resuscitated with endotracheal intubation, fluid boluses, prBC transfusion, and pressor support. The patient’s instability required emergent transfer to the operating room (OR).

The first operation was an exploratory laparotomy that revealed perforation of the gastric pouch adja- cent to the left lobe of the liver with a dark blood clot. The clot was gently removed, and active arte- rial bleeding was noted from the splenic artery. Direct pressure failed to provide adequate control of bleeding, and the Veith maneuver was employed.

The Veith maneuver is a technique for obtaining supraceliac aortic control. The lesser omentum is divided, and the stomach and distal esophagus are retracted to the left. Blunt, manual dissection around the gastroesophageal junction allowed it to be encircled with a Penrose drain and retracted laterally, which exposes the supraceliac aorta just below the diaphragmatic hiatus and allows for control with a clamp or direct pressure.

Arterial bleeding was then controlled; oversewing of the splenic artery followed. This operation was followed by delayed reconstruction with gastric pouch resection and esophagojejunostomy. Distal enteral feeding access and delayed abdominal wall closure were performed as well. Following closure, the patient developed a perihepatic abscess, which was managed uneventfully with placement of a drain by interventional radiology (IR). Patient A was discharged to a rehabilitation facility after a 1-month stay in our hospital.

**Patient B**

Patient B is a 53-year-old woman who presented as a referral from Gastroenterology for recurrent epigastric pain, refractory gastroesophageal reflux disease, dysphagia, and surgical history of RYGB 22 years prior to presentation. She stated that she previously used cocaine and smoked cigarettes, but did not currently use any drugs or tobacco products. The patient had maintained a 100-pound weight loss for nearly 20 years before developing an increase in hunger with mild dysphagia to solids. EGD revealed marginal ulcers, which were treated with proton pump inhibitors and sucralfate. The patient returned to prebypass weight within 2 years.

She was taken to the OR for laparoscopic excision of 2 large gastro-gastric fistulas, lysis of adhesions, and gastrostomy tube placement. She developed fever and tachycardia postoperatively, and upper gastrointestinal series confirmed a lateral gastric pouch leak. She was taken to the OR a second time for EGD and esophageal stent placement. The patient was discharged from the hospital after a 39-day stay complicated by recurrent fever, vomiting, and abdominal pain with multiple endoscopies for repositioning of the stent.

She returned to the hospital multiple times over the next 6 months for fever, vomiting, and abdominal pain—all managed nonoperatively. Eventually, the esophageal stent was removed endoscopically due to intractable abdominal pain and vomiting. Laparoscopic cholecystectomy was also performed after HIDA (hepatobiliary) scan revealed chronic cholecystitis. The patient was discharged but pre- sented to the ED 3 weeks later with epigastric pain radiating to the back, lightheadedness, diarrhea, and 6 episodes of hematemesis in 24 hours. The patient was admitted to the surgery inpatient service, but she soon began vomiting bright red blood and was transferred to the surgical ICU. The patient received 1 unit of pRBC after becoming tachycardic and hypotensive. IR was contacted for management of the upper gastrointestinal bleed, but patient load precluded transfer to the IR suite.

The patient was then taken to the OR for exploratory laparotomy where dense subhepatic adhe- sions to the gastric pouch were noted. Due to concern for marginal ulcer erosion into the proximal splenic artery, pressure was applied to the celiac trunk. Arterial pulsations were noted at the poste- rior aspect of the gastric pouch, but visualization of the bleeding site was difficult due to the liver adhe- sions. A partial left heptectomy was performed and a gastroscope was employed for better visual- ization of the bleeding vessel. This vessel, which was identified as the splenic artery, was oversewn for control of the hemorrhage.

The patient underwent a total of 5 operative proce- dures as she required additional second-look operations for a bile leak that healed conserva- tively. A partial colectomy was required followed by reconstruction with gastric pouch resection and esophagojejunostomy. A leak at the esophagojejunostomy was successfully treated with a fully cov- ered self-expanding metal stent. Patient B was dis-
Correspondence
Address to:
Andrew J. Jones, BS, BA, Department of Surgery, Augusta University Health, 1120 15th St, Bl-4070, Augusta, GA 30912 (ajones9@augusta.edu)

charged to a rehabilitation facility after a 1-month stay in our hospital.

Both patients survived despite massive transfusion requirements and prolonged hospitalization. Additionally, they both retained their spleens though Patient B suffered multiple splenic infarcts and was consequently immunized.

Discussion
As illustrated in the above cases, splenic artery erosion from marginal ulcers can precipitate severe gastrointestinal bleeding and lead to instability and life-threatening shock. Bariatric complications increase with patient age and time elapsed since the initial operation. Patients with complications often present acutely and are therefore treated by nonbariatric surgeons.

Commonly reported diagnoses include anastomotic leak, pulmonary embolism, internal hernia, small bowel obstruction, gastric band slippage or restriction, biliary disease, perforated ulcer with or without vessel erosion, and gastric outlet obstruction. Late complications include pouch enlargement, band erosion, gastric remnant syndrome, anastomotic stenosis, dumping syndrome, gastroesophageal reflux, and vitamin deficiencies. The majority of these complications do not progress to critical levels, and minimally invasive techniques are appropriate in most cases.

Despite multiple reports of gastric ulcer perforation following RYGB, there are few case reports detailing arterial erosion. Sidani et al describe a case in which the patient developed gross hematemia following RYGB. During exploratory laparotomy, the spleen appeared dusky and was excised allowing for angiographic embolization of the splenic artery. The authors proposed consideration of preoperative embolization to allow a safer surgical repair of the RYGB.

Bleeding marginal ulcers can be treated surgically with either open or laparoscopic procedures with identification and ligation of bleeding vessels. Sasse et al recount 7 individual case presentations of perforated marginal ulcer. Six required open or laparoscopic exploration with oversewing and omental patch. The seventh patient expired intraoperatively from multiple organ failure. Patients presenting without severe bleeding who maintain hemodynamic stability can be treated endoscopically while those presenting en extremis will typically require surgical intervention.

Conclusion
Although rare, massive upper gastrointestinal bleeding from ulcer erosion into the proximal splenic artery may require urgent and specific surgical therapy. Strong consideration should be given to interventional radiographic angiography for recurrent or initial severe upper gastrointestinal bleeds in RYGB patients. Our institution has established this protocol in light of the cases described above. Operative intervention, including the Veith maneuver for supraceliac aortic control, may be necessary if angiography fails or is not readily available. The bariatric and acute care surgeon should have a working knowledge of approaches to this particular life-threatening scenario.

References
Dexmedetomidine-Induced Adrenal Crisis in an Infant

Jeremy M. Loberger, MD; Robert S. Seigler, MD; and Michael G. Avant, MD

From the Internal Medicine and Pediatrics Residency Program, Greenville Health System, Greenville, SC (J.M.L.), and Department of Pediatrics, Division of Pediatric Critical Care, Greenville Health System, Greenville, SC (R.S.S., M.G.A.)

Abstract

Dexmedetomidine is a selective alpha-2 adrenergic agonist with sedative, analgesic, and anxiolytic effects. It has a similar structure to another sedative, etomidate, which is known to cause adrenal suppression. Therefore, there has been theoretical concern that dexmedetomidine may have the same effect. In this case report, we present a young infant who developed adrenal crisis shortly after receiving a high-dose dexmedetomidine infusion. To our knowledge, this incident is only the second case report documenting this potential side effect in the pediatric population and the first of such severity. The use of dexmedetomidine is increasing in pediatric patients. Therefore, it is important to publish this case to increase awareness of this potential side effect.

Dexmedetomidine (Precedex®, Hospira) is a selective alpha-2 adrenergic agonist. It was initially approved by the Food and Drug Administration in 1999 for sedation in mechanically ventilated adult patients, for periods less than 24 hours. In addition to its sedative effects, it also possesses mild analgesic and anxiolytic properties coupled with minimal respiratory depression.1

Use in pediatrics is currently off label, consistent with the use of many other sedatives in this patient population. Nonetheless, it has seen increasing usage in the past few years, primarily in procedural sedation. It is also used for sedation in mechanical ventilation and clinical situations requiring longer term sedation. Adult studies have also demonstrated utility as a narcotic sparing agent in postsurgical patients.2

Dosing regimens for dexmedetomidine are not well defined in pediatric patients. Limited data suggest that a suitable range is 0.1–2.0 mcg/kg/hr.3 Other publications have documented doses as high as 2.7 mcg/kg/hr.4,5

Adrenal crisis is a syndrome that occurs either with acute onset adrenal insufficiency or in a patient with chronic adrenal insufficiency who experiences significant physiologic stress. The syndrome is usually associated with deficiencies in both mineralocorticoids (eg, aldosterone) and glucocorticoids (eg, cortisol), but can also be partial. The most dangerous issues are caused by mineralocorticoid deficiency—hyponatremia, hyperkalemia, metabolic acidosis, and hypotension. Acute drops in serum sodium can result in seizures, and acute rises in potassium can result in cardiac dysrhythmias. Glucocorticoid deficiency causes hypoglycemia, fatigue, nausea, and muscle weakness. Significant hypoglycemia can also result in seizures. In severe cases, the patient may develop shock and cardiovascular collapse.6

In this case report, we present an infant who developed adrenal crisis following the use of high-dose dexmedetomidine over 11 hours for sedation in our Pediatric Intensive Care Unit (PICU). To our knowledge, this instance is only the second case report documenting adrenal crisis and only the second case documenting clinically significant adrenal side effects associated with this medication.

Case Description

A 49-day-old, ex-term male infant presented to our PICU with respiratory syncytial virus-induced bronchiolitis. The patient had no significant past medical history at the time of admission. After failing heated high-flow nasal cannula and CPAP (continuous positive airway pressure), he was intubated for persistent, severe respiratory distress and hypoxia.
Initially, continuous midazolam and fentanyl were used for sedation and analgesia. He required paralysis with continuous vecuronium shortly after intubation and intermittently as his course progressed.

On the day following intubation, two 2.5 mg (0.4 mg/kg/dose) doses of methylprednisolone were administered due to concern for a reactive airway component. No other steroids were used as his course progressed. He continued to require frequent rescue doses of midazolam and fentanyl for sedation. Adequate sedation was challenging, and he was trialed on continuous propofol, scheduled lorazepam, and scheduled methadone.

On hospital day 11 (mechanical ventilation day 9), he was transitioned to dexmedetomidine in hopes of decreasing narcotic and benzodiazepine cumulative dosing. An initial loading bolus of 3 mcg (0.5 mcg/kg) was administered followed by a continuous maintenance infusion at a rate of 3 mcg/kg/hr. The maintenance infusion rate was decreased to 2 mcg/kg/hr 6 hours later due to hypotension.

Approximately 11 hours after the infusion started, the patient had onset of generalized seizure activity. An electrocardiogram demonstrated right bundle branch block and junctional escape. Serum chemistry at that time showed sodium of 121 mMol/L, potassium of 9.8 mMol/L (nonhemolyzed), bicarbonate of 18 mMol/L, and glucose of 91 mg/dL. Random, nonstimulated serum cortisol at that time was 10 mcg/dL. Electroencephalogram confirmed generalized seizure activity. Dexmedetomidine was discontinued, and stress dose intravenous hydrocortisone was started in addition to antiepileptics and 3% saline. A lumbar puncture was performed, and studies were not indicative of meningitis.

By that afternoon, the patient’s serum sodium had normalized and seizure activity had terminated. Hydrocortisone was slowly tapered and ultimately discontinued over the next 4 days. The patient had a complete recovery and was discharged home on hospital day 29 without any steroids or antiepileptics.

**Discussion**

Etomidate is a sedative medication that is well known to cause adrenal suppression. The mechanism is direct inhibition of the 11β-hydroxylase enzyme in the adrenal cortex. Etomidate’s imidazole ring structure is responsible for this inhibition. As a result, there has been concern that dexmedetomidine could have similar effects on adrenal function. One animal study showed decreased serum cortisol and decreased cortisol response to adrenocorticotropic hormone stimulation following exposure to dexmedetomidine. However, studies in humans have largely shown no clinically significant impact on adrenocortical function, likely because dexmedetomidine causes adrenal suppression at concentrations above $10^{-6}$ M while the therapeutic concentration in humans is $10^{-9}$ M.

There is at least 1 case report of transient adrenal suppression occurring with clinical use in a pediatric patient. In that report, dexmedetomidine was administered to a 10 kg pediatric burn patient for 6.5 days with a maximum dose of 2.7 mcg/kg/hr. The patient developed transient adrenal suppression 4 days after the infusion was discontinued. His presenting symptoms were lethargy and hypotension. This use is similar to our maximum dose, but a much longer duration than in our case.

Our patient had a more rapid onset of symptoms with significant electrolyte abnormalities and seizures after a shorter duration of treatment. This timeline correlated directly with the addition of dexmedetomidine only 11 hours earlier and corrected rather rapidly after it was discontinued. His presenting symptoms were lethargy and hypotension. This use is similar to our maximum dose, but a much longer duration than in our case.

It is important to note that the serum cortisol would be expected to be much higher in the setting of this patient’s critical illness. Furthermore, the serum glucose was normal. This finding argues for partial adrenal insufficiency primarily impacting mineralocorticoid production rather than complete insufficiency with concomitant glucocorticoid deficiency. It is possible that continuation of the infusion may have ultimately resulted in complete adrenal insufficiency.

The infusion rate administered to our patient was higher than what is commonly reported in the literature. The initial higher dose of 3 mcg/kg/hr was chosen given the patient’s increased threshold for sedation noted with previous medications. After decreasing to 2 mcg/kg/hr, the dosing was within commonly accepted dosing ranges. The high dose coupled with his critical illness may
DEXMEDETOMIDINE-INDUCED ADRENAL CRISIS

explain the profound impact on adrenocortical function. In follow-up, our patient has not experienced recurrence of his adrenal insufficiency that would suggest an underlying adrenal pathology.

It is plausible that his serum drug concentrations rose above the 10^{-6} M level known to result in adrenal suppression. There was no suggestion of hepatic or renal impairment that could have blunted metabolism or clearance of the drug resulting in higher serum concentrations. Our patient had not been treated with high-dose or prolonged courses of steroids and was not receiving any other medications known to cause adrenal suppression. Thus, the most likely etiology for his adrenal crisis is dexmedetomidine.

Conclusion

This case report suggests that, contrary to what is reported in the current literature, the potential exists for considerable adrenocortical impact from high-dose dexmedetomidine. As a result, caution should be exercised when this medication is used at high doses or in patients with possible underlying adrenal pathology.

References


Correspondence

Address to: Jeremy Loberger, MD, Greenville Health System, Internal Medicine/Pediatrics, 701 Grove Rd, Greenville, SC 29605 (jloberger@ghs.org)
Case Studies

Radiographic Evidence of Diffuse Large B-cell Lymphoma Presenting as Carpal Tunnel Syndrome

Anthony J. Horton, BS, and Jeffrey R. Wienke, MD

From the University of South Carolina School of Medicine Greenville, Greenville, SC (A.J.H., J.R.W.), and Department of Radiology, Greenville Health System, Greenville, SC (J.R.W.)

Abstract

Any space-occupying lesion in the carpal tunnel can present with median nerve compression and the symptomatology of carpal tunnel syndrome (CTS). Typically, history and physical examination reveal sufficient findings to warrant further investigation with electrophysiologic testing; imaging studies, however, are not routinely considered. Here, we present a case of CTS resulting from carpal tunnel infiltration by a soft-tissue, non-Hodgkin lymphoma as evidenced by non-contrast MRI (magnetic resonance imaging).

Case Description

M.R. is a 78-year-old Caucasian man with a past medical history of hypertension, hyperlipidemia, hemochromatosis, and left testicular lymphoma with disease-free status following orchiectomy, chemotherapy, and radiation therapy that began 3 years prior to presentation. Initially, M.R. presented to his primary care provider with right hand weakness, tingling, and occasional numbness. Physical examination was notable for reproducibility of paresthesias with wrist flexion, subtle thenar atrophy, and mild anterior wrist swelling without erythema.

Diagnostic work-up, including nerve conduction studies, revealed delayed nerve conduction of the median nerve across the carpal tunnel along with mild reduction in conduction velocity along the ulnar nerve at the cubital tunnel. The patient subsequently underwent elective right carpal and cubital tunnel release, during which the median nerve was found to be intact with nonspecific hyperemic changes beneath the transverse carpal ligament. Postoperative care was notable for acute, same-day right hand pain that was subsequently treated with pregabalin on an outpatient basis.

In the ensuing weeks after carpal and cubital tunnel release, the patient experienced moderate resolution of weakness and paresthesias of his right hand; however, on postoperative week 6, M.R. pre-
presented to his primary care physician with recurrent edema, new erythema, and significant pain in his right wrist with radiation into the hand in a median nerve distribution. Physical examination revealed a well-healed surgical scar with no signs of infection or dehiscence, but sensory loss along the distribution of the distal median nerve was noted.

Subsequent non-contrast MRI (magnetic resonance imaging) of the right upper extremity revealed mild median nerve thickening with extensive, lobulated soft-tissue abnormalities throughout the hand, particularly at the distal ulnar margin of the thenar eminence surrounding the flexor tendons. Insinuating extensions projected between the second, third, and fourth metacarpals. Lobulated soft-tissue abnormalities were further noted in the dorsum of the first web space and surrounding the hypothenar musculature.

Compared to surrounding musculature, this abnormal tissue presented with moderately increased signal intensity on T1 and T2 images (Figs. 1–2). Additionally, proton density fat saturation images of the lobulated masses revealed mildly increased signal compared to surrounding soft tissue (Fig. 3). No bony destruction or erosive changes were identified. Ultimately, the differential diagnosis based on the imaging studies included a recurrence of soft-tissue lymphoma, fibromatosis, or postoperative infection contributing to tenosynovitis.

Given the patient’s history of testicular lymphoma, new imaging findings, acute initial onset of symptoms, and recurrence of painful swelling at the right wrist following carpal and cubital tunnel release, an excisional biopsy of the mass was performed. Biopsy samples identified a diffuse large B-cell lymphoma, which likely represented a recurrence of his prior testicular lymphoma.

Whole-body nuclear medicine positron emission tomography (PET) with overlying computed tomography (CT) images were obtained for staging purposes. Multifocal hypermetabolic activity was noted throughout the right upper extremity, including the right wrist and numerous lymph nodes tracking to the right axilla. Further hypermetabolic activity was noted in a right adrenal mass, proximal right tibial shaft, distal left thigh in the anteromedial subcutaneous tissue, and the left orbit (Fig. 4). With this advanced stage and tumor burden, chemotherapy with rituximab, etoposide, steroid (methylprednisolone), Ara-C (cytarabine), and platinum (cisplatin) (R-ESHAP therapy) and palliative upper extremity radiation therapy were initiated.

Discussion

Lymphomas are an assorted group of malignancies classically arising from lymph nodes or lymphatic tissues such as the spleen, Waldeyer’s ring, and the thymus. However, extranodal presentations of non-Hodgkin lymphomas occur at reported incidence rates of 25%–40%. When they occur, extranodal lesions are more common in...
men and have been documented in almost every organ system.3

Most commonly, extranodal presentations of non-Hodgkin lymphoma occur with simultaneous involvement of lymphatic structures, and an extranodal site is only considered to be the primary lesion if no additional evidence of neoplasia is discovered during staging.4 Even so, the presence of a tumor or mass outside of lymph node tissue is often not considered a lymphoma until after tissue biopsy and histopathology establish the diagnosis, with the most common histological subtypes being follicular and diffuse large B-cell lymphomas. Specific to this case, only 0.2% of extranodal non-Hodgkin lymphomas present with hand involvement.5

Imaging characteristics of lymphoma vary depending on location and specific subtype of disease. Computed tomography is the mainstay of imaging, specifically for its role in tumor staging. However, MRI has particular utility in central nervous system lymphomas, and ultrasound (US) techniques can be used to access disease with lymph node involvement.6

For the patient presenting with median nerve compression, imaging studies are neither explicitly necessary nor routinely ordered. Still, imaging may be useful when there is a suspicion for local structural disease such as bony deformity, primary bone or joint disease, or tumor. Wrist films and CT are only indicated to evaluate carpal tunnel stenosis or bone tumors, with MRI or high-frequency US being more useful for direct visualization of the median nerve and other soft tissues.

Use of MRI or US is appropriate to identify a space-occupying lesion in the soft tissue such as a tumor, ganglion cyst, lipoma, or muscle fiber hypertrophy, with MRI in particular having a 96% sensitivity and 33%–38% specificity for this purpose.7 More recently, several studies have demonstrated the utility of ultrasonography to detect CTS due to the apparent increase in cross-sectional area of the median nerve in the diseased state, though a defined cut-off for diagnosis has not been adequately determined.8

For this case of rapid recurrence of CTS following surgical correction, detailed imaging of the affected hand, including MRI of the wrist or US of the carpal tunnel, was warranted to evaluate for atypical etiologies of median nerve compression, especially given the patient’s history of lymphoma and lack of structural abnormalities on

Figure 3
Axial proton density fat saturation MRI demonstrates extensive, lobulated soft-tissue abnormality throughout the right hand, particularly at the distal margin of the thenar eminence surrounding the flexor tendons insinuating between the second to fourth metacarpals. The lesion is isointense to surrounding soft-tissue structures.

Figure 4
Whole-body Nuclear Medicine Positron Emission Topography with overlying Computed Tomography (NM PET/CT) demonstrates multifocal hypermetabolic activity in the right hand, right upper-extremity lymph nodes, right adrenal gland, and subcutaneous proximal right thigh among other scattered foci.
physical exam. Review of the literature reveals that this instance is not an isolated presentation of disease, as there have been case reports of other neoplastic processes, including T-cell lymphoma and primary non-Hodgkin lymphoma, infiltrating the distal median nerve and leading to CTS.9,10

Consistent with the images in this case, nonosseous musculoskeletal lymphomas present with isointense or intermediate hyperintensity on T1 and T2 images when compared to surrounding muscle and fat tissue. This finding is reiterated on proton density fat saturation MR images, where soft-tissue lymphoma may be isointense to surrounding soft tissues as in this case.

Fibromatosis and tenosynovitis were considered in the differential of this patient’s imaging findings. However, fibromatosis more classically presents with isointense to intermediate hyperintensity on both T1 and T2 images when compared to surrounding muscle and fat tissue, while tenosynovitis may present with intermediate signal debris in the tendon sheath itself plus high intensity on T2 weighted images.6

**Conclusion**

Neoplastic processes, including primary and metastatic non-Hodgkin lymphomas, can infiltrate the wrist, compress the median nerve, and present as CTS; thus, neoplastic disease should remain in the differential diagnosis for all patients, particularly when disease is unilateral. When an infiltrative process is suspected, MRI is the imaging modality of choice, though high-frequency US of the median nerve traversing the carpal tunnel is another viable option.

**References**

Management of Brujeria, a Culture-Bound Syndrome

Joseph T. Mingoia, MD, and Taral R. Sharma, MD, MBA

From the Department of Psychiatry, Carilion Clinic, Roanoke, Va (J.T.M.), and University of South Carolina School of Medicine Greenville, Greenville, SC (T.R.S.)

Abstract

In medicine, a culture-bound syndrome is an array of aberrant behavior phenomena often recognized as illness by most participants of a particular culture. Although considered uncommon in the United States (US), various culture-bound syndromes have been reported in Hispanic populations. The population of Hispanic immigrants in the US is on the rise, and the presence of such syndromes should not be overlooked. Presently, published literature describing culture-bound syndromes, specifically Brujeria—Spanish for witchcraft—is very limited. The aim of this report is to provide a detailed description of a patient with Brujeria, including presentation and subsequent psychiatric and medical management.

A culture-bound syndrome is an array of aberrant behavior phenomena often recognized as illness by most participants of a particular culture.1 Although uncommon in the United States (US), various culture-bound syndromes have been reported in Hispanic populations.2 According to the US Census Bureau, Hispanics constitute the nation’s largest ethnic minority (55 million/17%).3 As such, the presence of such syndromes should not be surprising or overlooked. Presently, published literature describing culture-bound syndromes, specifically Brujeria—the Spanish word for witchcraft—is very limited.4 This case report describes the presentation and management of a 27-year-old Honduran woman with Brujeria.

Case Description

A 27-year-old Honduran woman with a medical history significant for chronic migraines presented to our Emergency Department (ED) with an intractable headache. The patient immigrated to the US 6 years prior and spoke little English. Through a Spanish-speaking, hospital-based interpreter, the patient reported severe (10, on a pain scale of 10), intermittent headaches, usually located in her bitemporal regions, that progressively worsened 4 days prior to ED presentation.

The headaches were uncontrolled by over-the-counter naproxen and caused photophobia, blurry vision, and pain around her right eye. The patient also complained of bilateral leg weakness with sharp, stabbing, and squeezing pain in both legs. She was admitted to the medical service and underwent a head CT (computed tomography), lumbar puncture with cerebrospinal fluid exam, syphilis screen, thyroid panel, comprehensive metabolic profile, complete blood count, urinalysis, urine drug screen, and urine pregnancy test—all of which were inconclusive of any acute medical problems.

Within a short time (1–2 days), the patient started displaying symptoms of depression and Psychiatry was consulted. The patient reported anhedonia, poor concentration, guilt, and low energy, which she attributed to financial constraints and unemployment. She also reported paranoia that her neighbors and friends from Honduras were talking about her. She denied any manic symptoms, any history of suicidal or homicidal ideations, and any alcohol or illicit substance abuse.

The patient’s boyfriend said that during her episodes at home she would hold onto the walls to walk, did not appear to know where she was, and would often talk to people who were not present and motion as if speaking to someone on the telephone. The patient acknowledged having visual hallucinations, specifically of a young child with a pale face lying next to her in bed.
At this point, one of the hospital interpreters disclosed an earlier event when the patient was visited by her spiritual advisor. According to the interpreter, shortly after the spiritual advisor’s visit, the patient began writhing and twisting as if being attacked or stabbed. The interpreter went on to explain how this reaction was consistent with Brujeria from their home culture. The patient admitted to feeling possessed during her advisor’s visit and later disclosed that her aunt practiced witchcraft and had persecuted others in a similar fashion.

Mental status examination revealed the patient to be in mild distress, but cooperative, alert, and oriented to person, place, and time. There were no fluctuations in consciousness, and no deficits were noted following the mini-mental state examination. Differential diagnosis included Brujeria, somatoform disorder, conversion disorder, major depression disorder, generalized anxiety disorder, and panic disorder.

Both patient and boyfriend believed in Brujeria as a culture-bound syndrome and associated her current symptoms with this syndrome. The patient elected prayer (led by the Psychiatric consultation team) and spiritual healing over medication management; no psychotropic medications were administered. Following the prayer, the patient’s headache and leg weakness improved significantly. The patient was discharged on hospital day 4 and encouraged to pray with her boyfriend, seek the help of their spiritual advisor, and follow-up with her primary care physician.

Discussion

Each human society has its own distinct body of beliefs. Brujeria is a specific type of witchcraft associated with Afro-Latin religious systems that frequently entails invocation of various spells and deities for either good or evil. It is believed that life problems and/or psychosomatic complaints may result from Brujeria. The practice of Brujeria (eg, rituals, spellwork, healing, etc.) is diverse and dependent on location and dominant religion. Published literature on the treatment of culture-bound syndromes is sparse, especially in the US. Reported treatments, however, include psychoanalysis, cognitive behavioral therapy, and incorporation of culture-specific treatments from values prevalent in the population (eg, shaman, priest, curandero, spiritual leader, family, etc.).

In this case report, the value of the interpreter should not be underestimated. If available, hospital-based and/or professional interpreters should be utilized, as one of our interpreters provided valuable information regarding the symptoms that became manifest in the presence of the patient’s spiritual advisor, ultimately leading to the identification of the cultural association. Knowledge of the social context is central to diagnosing the syndrome. Without understanding contextual association, many similar presentations could go unrecognized. If a symptom cluster does not represent a normal response and testing is inconclusive, we recommend that clinicians consider asking patients if they have a preconceived notion of a cultural cause for their condition. The clinician should also assess if there are any language barriers in eliciting symptoms or understanding the patient’s expressions. If so, once again, we recommend use of an interpreter.

We do, however, recognize that our case was unique, as most professional interpreters do not have the training or expertise to conduct an assessment of complex psychological issues, nor should they be expected to assess the patient’s religious behavior. Most hospitals have the ability to consult staff chaplains; this group my prove helpful to the clinician and patient, as they typically have expertise and experience in working with diverse religious populations and persons presenting with various spiritual values and beliefs.

Another important aspect exposed in this case report was the need for open communication between the clinicians (psychiatry and medicine) and the patient. Once our patient believed Brujeria to be the cause of her illness and symptoms, specific conversations regarding her expectations and preferences for medications or therapy followed, ultimately ending in no medications being administered. Some patients may believe the psychological disorder to be somatically based and should be treated with medication, while others may view medication as too simplistic and prefer psychotherapy. The earlier the clinician can involve the patient in a treatment/management conversation so as to establish realistic expectations for rate of recovery, the better.

Conclusion

In conclusion, we present a case of patient suffering from Brujeria, a culture-bound syndrome considered uncommon in the US and rarely described in the literature. As the US immigrant population continues to grow, so does the need for clinicians to increase their cultural awareness of possible culture-bound syndromes.
References


Levamisole-Induced Necrosis Syndrome Associated With Cocaine Use

Richard O’Neal, MD, and Sheena Henry, MD

From the Department of Medicine, Greenville Health System, Greenville, SC (R.O., S.H.)

Abstract

With the increasing prevalence of levamisole contamination of cocaine, there has been a concurrent rise in patients presenting with a vasculitis-like syndrome characterized by purpura, hemorrhagic bullae, and skin necrosis. The following case describes a 43-year-old woman who presented with rapidly worsening painful purpura on her extremities and nose, leukopenia, and perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA) following cocaine use. She developed extensive necrosis necessitating multiple wound debridements but eventually recovered with supportive care and cessation of cocaine.

Case Description

A 43-year-old African American woman with a history of sarcoidosis and chronic anemia presented with a 4-day history of painful areas of deep violet discoloration that had been expanding bilaterally along the lower extremities. Examination revealed broad, circumferential areas of intensely warm and painful purpura (Fig. 1). In addition, cutaneous necrosis was noted at the tip of the nose (Fig. 2) and helix of the ears.

Figure 1
Purpura fulminans with hemorrhagic bullae associated with levamisole-contaminated cocaine.

With the continued demand for cocaine, and an estimated 1.5 million active users in the United States (US), various adulterants are added during its production and distribution. In 2003, levamisole was first detected in cocaine, and by 2014, the US Drug Enforcement Administration reported up to 78% of cocaine in the US now tested positive for levamisole. As an additive, levamisole is thought to potentiate the stimulatory effect of cocaine by blocking the reuptake of dopamine in presynaptic neurons.

Historically, levamisole was authorized for use as a chemotherapy drug, as well as a treatment of rheumatoid arthritis and pediatric nephrotic syndrome. Feared complications from levamisole use were first documented in 1978 and included agranulocytosis, arthritis, skin ulcers, and cutaneous vasculitis. Due to increasing concerns over side effects, the Food and Drug Administration removed the drug from the market in 2000. Although levamisole is still available as a veterinary antihelminthic, it has been adopted by the drug trade as a cutting agent. Whereas levamisole-induced necrosis had previously been an iatrogenic side effect, by 2009 this complication was experiencing a resurgence due to its correlation with cocaine use.
On admission, the patient was anemic and leukopenic (Table 1). Review of records revealed the patient had a history of intermittent leukopenia, a work-up for which had been negative just 5 months before her current presentation. On admission, intravenous methylprednisolone was administered to treat a possible leukocytoclastic vasculitis.

During the first 24 hours of admission, the purpuric lesions worsened, with the patient developing large bilateral hemorrhagic bullae along the dorsal portions of the lower extremities. On day 2 of hospitalization, a venous duplex was negative for the presence of deep vein thromboses. A subsequent vasculitis work-up (Table 2) revealed elevated perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA); however, a skin biopsy revealed only necrosis without evidence of vasculitis.

Upon further investigation, the patient reported that 3 days prior to admission she had begun using crack cocaine again. Review of the literature at that time revealed similarities to Levamisole-Induced Necrosis Syndrome (LINES), given the positive p-ANCA markers, recent cocaine use, and cutaneous symptoms. The patient was provided supportive care with hydration, wound care, and a long steroid taper. After 9 days of hospitalization, the patient was discharged home with physical therapy. At time of discharge, the purpura had improved, but the large bullae persisted.

Sixteen days after discharge, the patient was readmitted to the hospital after rupture of the large bullae with complaints of purulent drainage. X-rays of the lower extremities revealed diffuse soft-tissue swelling bilaterally with evidence of gas within the soft tissue. A new area of purpura, now also with concern for infection, was even present on the right upper extremity. Surgery was consulted, and the patient was started on vancomycin, meropenem, and metronidazole. Tissue cultures taken from her wounds ultimately revealed Escherichia coli. A muscle biopsy on day 4 of hospitalization revealed necrotic skeletal muscle with patchy acute inflammation, necessitating extensive debridement by vascular surgery twice during her hospital stay (days 4 and 19) and skin grafting. Below-knee amputation was considered due to the extent of necrosis, but was able to be avoided. After 44 days of hospitalization, the patient was discharged with close primary care provider and wound care follow-up. Eleven months posthospitalization, the patient reported continued abstinence from cocaine without recurrence of purpura or necrosis; her leg wounds resolved, but there was autoamputation of the tip of her nose.

**Discussion**

LINES, also known as levamisole-induced pseudovasculitis, is an entity that has only been characterized within the last decade.\(^2\) LINES has a gender partiality for females (3:1), with a mean age of onset of 44 years.\(^2\) Although definitive diagnostic criteria have not yet been established, cases of LINES share certain clinical features.\(^5,10\)

![Necrosis of the nose associated with levamisole-contaminated cocaine.](image)
As described in this case, affected patients often have a tender rash of purpuric lesions on the extremities, nasal tip, ears, as well as on the trunk of the body and the digits of the hands and feet.\textsuperscript{2,6,10} The most severe cases present with the tender retiform coalescing purpura, hemorrhagic bullae, and skin necrosis as seen in this patient.\textsuperscript{4} In some instances, the degree of necrosis may necessitate amputation.\textsuperscript{4}

Laboratory analysis often reveals elevated inflammatory markers, agranulocytosis, anti-neutrophil cytoplasmic antibodies, antiphospholipid antibodies, and antihuman elastase antibodies.\textsuperscript{2,3,6,13} Given the chronicity of cocaine use in this patient, there may have been an element of levamisole that was causing her chronic leukopenia, which had yielded a negative work-up in the months prior to this hospitalization. Also, the patient later revealed that she had small purpuric lesions in the past that were less severe and had resolved without intervention. The patient’s positive p-ANCA and antimyeloperoxidase antibodies, although not specific to LINES (Table 3), are often presenting factors of this syndrome as well.\textsuperscript{2,3,6,7} Though not available at all institutions, urine or blood gas chromatography and mass spectrometry within 48 hours can often detect levamisole, but is not required for diagnosis.\textsuperscript{3,6} Pathologic findings may vary from leukocytoclastic vasculitis of the small vessels to thrombotic microangiopathy.\textsuperscript{2,6} However, biopsies often reveal only gross tissue necrosis, leading some to classify this disease as a pseudovasculitis.\textsuperscript{2}

The vast majority of illicit drug users exposed to levamisole do not develop clinical symptoms; however, those who do may require hospitalization and supportive care to minimize the morbidity associated with tissue necrosis and agranulocytosis. The mainstay of treatment is cocaine cessation.\textsuperscript{1,3,4,6,11}

**Conclusion**

With the increasing prevalence of levamisole-contaminated cocaine and the number of illicit drug users potentially exposed, it is crucial that healthcare providers be aware of this condition. Though some laboratory tests are of value (p-ANCA, antihuman elastase antibodies, antiphospholipid antibodies), the most important aspect of diagnosis is recognition of clinical exam findings in the presence of cocaine exposure. Through early recognition and diagnosis, healthcare providers can not only initiate appropriate supportive care early, but also educate patients on the importance of cocaine cessation.
Correspondence
Address to:
Richard O’Neal, MD,
Greenville Health
System, Department
of Medicine, 5th Floor
Support Tower, 701
Grove Rd, Greenville,
SC 29605 (roneal@ghs.org)

References
On the national stage, GHS’ Cancer Institute is making breakthroughs in cancer research and treatment—and making innovative, comprehensive care available close to home for upstate patients:

• In 2014, 34 programs were lauded by the National Cancer Institute as a leader in community-site care delivery and research: GHS’ Cancer Institute is the only community-based program originating in SC to attain this distinction

• GHS’ Institute for Translational Oncology Research includes a Phase I clinical research unit, a biorepository services platform, and proteomics and genomics capabilities: Thus far, it has enrolled in excess of 1100 patients in 150 studies, including 17 first-in-human trials, with 12+ drugs moving to FDA approval and 40+ articles published

• GHS’ Blood and Marrow Transplant Program, the first in SC to receive accreditation for autologous transplantation, provides both autologous and allogeneic transplants from matched related, unrelated and haplotype donor sources

• GHS’ Center for Integrative Oncology and Survivorship, one of the first programs of its kind in the nation, offers evidence-based complementary therapies in addition to conventional cancer treatment and research studies

For more information, please call (864) 455-7070.
Opinion
89 Monoclonal Antibodies, Blood-Brain Barrier and Disability in Multiple Sclerosis: Time for Combination Therapies by J Avasarala

Teachable Moment
92 Do I Really Need to Stop Taking Estrogen? by CW Fox et al

Value Vignette
94 Choosing High-Value Care in Suspected Lower Extremity Deep Vein Thrombosis by M Won and S Connelly

Special Article
97 Perceptions of and Preferences for a Mobile Health Clinic for Underserved Populations by M Gillispie et al

Original Research
105 The Gynecology and Obstetrics Fundamentals of Residency Internship Training (GO FOR IT) Trial by FS Nuthalapaty et al

113 Blood Loss and Transfusions After Pericardial Closure Using a Porcine-Derived Extracellular Matrix by TG Johnson et al

117 Impact of Methicillin-Resistant Staphylococcus aureus (MRSA) Decolonization Protocol on Colonization and Infection Rates in a Level III Neonatal Intensive Care Unit by M Griffin et al

121 Does Comprehensive Dementia Education Impact Self-Efficacy Among Family Caregivers in the Community? by X Pan et al

126 Insurance Status of Deceased Organ Donors by JD Cull et al

Case Studies
130 Catastrophic Upper Gastrointestinal Bleed in Roux-en-Y Gastric Bypass Patients From Ulcer Erosion Into the Splenic Artery: Details of Rapid Surgical Management by AJ Jones et al

133 Dexmedetomidine-Induced Adrenal Crisis in an Infant by JM Loberger et al

136 Radiographic Evidence of Diffuse Large B-cell Lymphoma Presenting as Carpal Tunnel Syndrome by AJ Horton and JR Wienke

140 Management of Brujeria, a Culture-Bound Syndrome by JT Mingoia and TR Sharma

143 Levamisole-Induced Necrosis Syndrome Associated With Cocaine Use by R O’Neal and S Henry