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<th>Specific disease/condition</th>
<th>Contact information (name, phone number, and e-mail address)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesiology</td>
<td>Chronic obstructive pulmonary disease, asthma (adult)</td>
<td>Beemnet Amare 214-818-2526 <a href="mailto:Beemnet.Amare@BSWHealth.org">Beemnet.Amare@BSWHealth.org</a></td>
</tr>
<tr>
<td>Asthma and pulmonary disease</td>
<td>Breast, ovarian, endometrial, prostate, brain, lung, bladder, colorectal, pancreatic, and head and neck cancer, hematological malignancies, leukemia, multiple myeloma, non-Hodgkin’s lymphoma; melanoma vaccine; bone marrow transplant</td>
<td>Frani Crockett, RRT 214-820-5829 <a href="mailto:Frani.Crockett@BSWHealth.org">Frani.Crockett@BSWHealth.org</a> 214-818-7899 Courtenay Patenaude, BS <a href="mailto:Courtenay.patenaude@BaylorHealth.org">Courtenay.patenaude@BaylorHealth.org</a></td>
</tr>
<tr>
<td>Cancer</td>
<td>Pancreatic islet cell transplantation for type 1 diabetics, who either have or have not had a kidney transplant</td>
<td>Lorie Estrada 214-820-3416 <a href="mailto:Lorie.estrada@BSWHealth.org">Lorie.estrada@BSWHealth.org</a></td>
</tr>
<tr>
<td>Diabetes (Dallas)</td>
<td>Type 1 and type 2 diabetes, cardiovascular events</td>
<td>Beemnet Amare 214-818-2526 <a href="mailto:Beemnet.Amare@BSWHealth.org">Beemnet.Amare@BSWHealth.org</a></td>
</tr>
<tr>
<td>Diabetes (Fort Worth)</td>
<td>Type 2: cardiac events</td>
<td>Trista Bachand, RN 817-922-2587 <a href="mailto:trista.bachand@BSWHealth.org">trista.bachand@BSWHealth.org</a></td>
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<td>Emergency Medicine</td>
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<tr>
<td>Gastroenterology</td>
<td>Inflammatory bowel disease</td>
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<tr>
<td>Heart and vascular disease (Dallas)</td>
<td>Aortic aneurysm; coronary artery disease, hypertension, poor leg circulation, heart attack, heart disease, congestive heart failure, angina, carotid artery disease, familial hypercholesterolemia, renal denervation for hypertension, diabetes in heart disease, cholesterol disorders, heart valves, thoracotomy pain, stem cells, critical limb ischemia, cardiac surgery associated with kidney injury, pulmonary hypertension; Heart and lung transplant, mechanical assist device such as LVAD</td>
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<td>Atrial fibrillation, atrial fibrillation post PCI</td>
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<tr>
<td>Heart and vascular disease (Legacy Heart)</td>
<td>At risk for heart attack/stroke; previous heart attack/stroke/PCI; cholesterol disorders; atrial fibrillation; obesity/obese; other heart-related conditions</td>
<td>Angela Germany 469-800-6409 <a href="mailto:Ihrresearch@baylorhealth.edu">Ihrresearch@baylorhealth.edu</a></td>
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<td>Tina Worley, RN, BSN 469-814-4712 <a href="mailto:Christina.Worley@BSWHealth.org">Christina.Worley@BSWHealth.org</a></td>
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</tr>
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</tr>
</tbody>
</table>
Early experience with digital advance care planning and directives, a novel consumer-driven program

Robert L. Fine, MD, Zhiyong Yang, PhD, Christy Spivey, PhD, Bonnie Boardman, PhD, and Maureen Courtney, APRN, PhD

Barriers to traditional advance care planning (ACP) and advance directive (AD) creation have limited the promise of ACP/AD for individuals and families, the healthcare team, and society. Our objectives were to determine the results of a digital ACP/AD through which consumers create, store, locate, and retrieve their ACP/AD at no charge and with minimal physician involvement, and the ACP/AD can be integrated into the electronic health record. The authors chose 900 users of MyDirectives, a digital ACP/AD tool, to achieve proportional representation of all 50 states by population size and then reviewed their responses. The 900 participants had an average age of 50.8 years (SD = 16.6); 84% of the men and 91% of the women were in self-reported good health when signing their ADs. Among the respondents, 94% wanted their physicians to consult a supportive and palliative care team if they were seriously ill; nearly 85% preferred cessation of life-sustaining treatments during their final days; 76% preferred to spend their final days at home or in a hospice; and 70% would accept attempted cardiopulmonary resuscitation in limited circumstances. Most respondents wanted an autopsy under certain conditions, and 62% wished to donate their organs. In conclusion, analysis of early experience with this ACP/AD platform demonstrates that individuals of different ages and conditions can engage in an interrogatory process about values, develop ADs that are more nuanced than traditional paper-based ADs in reflecting those values, and easily make changes to their ADs. Online ADs have the potential to remove barriers to ACP/AD and thus further improve patient-centered end-of-life care.

Knowledge of patient treatment preferences in the setting of terminal or irreversible illness leaving a person unable to communicate is important for young and old alike. The young and healthy may suddenly experience a catastrophic event permanently impairing all communication (Terri Schiavo is but one example). Serious illness impairing communication is naturally more common among elders, whose numbers are expected to double by 2030 (1), and 70% will lack decision-making capacity at the time decisions near the end of life are needed (2). In response to these realities, advance care planning (ACP) leading to advance directives (ADs) has been encouraged by law since the Patient Self-Determination Act of 1990. Yet, the 2014 Institute of Medicine report Dying in America (3), while also encouraging ACP, noted that the promise of ACP has not been met, with estimates suggesting that 30% or fewer individuals have an AD (4–6), and even when an AD is created, it is not easily available. Chiarchiaro, Arnold, and White recently proposed “next-generation” ACPs utilizing web-based technologies (7). We report on early experience with one such technology.

BENEFITS AND BARRIERS: THE CURRENT STATE OF ADVANCE CARE PLANNING

Seriously ill patients have distinct value preferences about treatment near the end of life, such as freedom from pain, peace with God, having their affairs in order, and dying at home as opposed to in the hospital (8). In the setting of terminal illness, 77% of persons indicated that they would not want to be placed on a mechanical ventilator to gain 1 month of life, and 86% preferred to die at home (9). Yet, 58% of patients die in the hospital, another 20% in nursing homes, and only 22% die at home (10).

This discordance between what patients want and what they get near life’s end is associated with high suffering (11) and unwanted and nonbeneficial treatments that prolong dying (12). Such “wrong medicine” also imposes significant costs on patients and families (13, 14) as well as society, with 25% to 30% of Medicare funds spent on the 5% of the Medicare population in the last year of life (15). These costs are not sustainable long term, as we currently take $3 out of Medicare for every $1 we pay in (16).

On the other hand, treatment preferences for life’s last chapter are more likely to be followed with lower family stress, anxiety, and depression in the presence of an AD (17, 18). Serious illness ACP conversations between physicians and patients lessen intensive treatment and lower expenditures, yet do not increase mortality (19). ACP benefits in the nursing home setting are similar (20), and AD utilization correlates with significantly lower levels of Medicare spending, a lower

From the Office of Clinical Ethics and Palliative Care, Baylor Scott and White Health, Dallas, Texas (Fine); and the College of Business (Yang, Spivey), College of Engineering (Boardman), and College of Nursing and Health Innovation (Courtney), The University of Texas at Arlington, Arlington, Texas.

Corresponding author: Robert L. Fine, MD, Office of Clinical Ethics and Palliative Care, Baylor Scott and White Health, 3600 Gaston Avenue, Suite 605, Dallas, TX 75246 (e-mail: robertf@baylorhealth.edu).
likelihood of in-hospital deaths, and increased hospice use in regions characterized by higher levels of end-of-life spending (21).

With end-of-life treatment deficits so clear and the ability of ACP to improve these deficits, why don’t most people have ADs? Reasons include lack of awareness, the falsehood that families know the person’s wishes anyway, the equating of ADs with limiting treatment, or a belief that creating an AD is complicated, expensive, or requires a lawyer or physician (2, 22). None of these statements is true.

For example, the Institute of Medicine notes the success of Respecting Choices (www.gundersenhealth.org/respecting-choices), an ACP program relying on trained community volunteers rather than physicians (3). However, such facilitated ACP is resource intense (7). Might a user-friendly digital platform, not necessarily requiring physician involvement, empower consumers/patients to create their own advance care plans on their own time?

DEVELOPMENT OF DIGITAL PLATFORMS FOR ADVANCE DIRECTIVES

Various organizations and companies have experimented with web-based solutions to the deficits in ACP. For example, PREPARE (https://prepareforyourcare.org/) focuses primarily on elderly patients and the process of ACP, but it does not actually create an AD. On the other hand, the US Living Will Registry (http://www.uslivingwillregistry.com/) allows a person to download a living will, complete it as a paper document, scan it, purchase online storage, and send it on request to healthcare providers.

This article reviews experience with another online ACP/AD platform, MyDirectives (www.mydirectives.com), designed to overcome many of the barriers and obtain more of the benefits of ACP/AD creation. To the best of our knowledge, MyDirectives is the first digital ACP/AD platform combining the elements of patient values and reflection on treatment preferences with a living will and medical power of attorney. Each AD is generated based on the unique user responses to questions presented in a process similar to an actual interview. The platform explores why the person is creating an AD and then queries the person’s values before delving into specific treatment preferences. Some representative questions are: 1) What best describes your current medical condition and why are you creating an AD? 2) What is important to you if you are seriously ill and can’t make your wishes known? 3) If your health ever deteriorates due to a terminal illness, and your doctors believe you will not be able to interact meaningfully with your family, friends, or surroundings, which of the following statements best describes what you’d like to tell them? 4) Which of the following statements best describes your thoughts on cardiopulmonary resuscitation (CPR)? and 5) If it were possible to choose, where would you like to spend your final days? The MyDirectives platform allows users to request the most intensive medically appropriate treatment, comfort-only treatment, or any nuanced variation in between. Users may incorporate audio and video messages into their ACP.

The result is an individualized ACP created, stored, and retrievable from the cloud at any time and from any place with Internet access, and the consumer is not charged for these services. The site prompts annual review of the directive, and to our knowledge, MyDirectives is currently the only digital ACP tool that can digitally integrate into any electronic health record, health information exchange, or patient portal.

METHODS

We analyzed a deidentified dataset provided by the company containing aggregated information from 900 US users of MyDirectives, randomly sampled proportionate to the population of each state, to represent the experience across multiple states. Responses were summarized through descriptive statistics. In addition to the ACP responses, data regarding demographics and revision of the ACP were gathered.

RESULTS

Respondents had an age range of 18 to 92 years (mean 50.8 ± 16.6). In this sample, 47.1% were <50 years old, and 84.3% of the men and 91% of the women were in self-reported good health.

Table 1 summarizes respondents’ choices related to the last stages of life. A standard definition of palliative care is offered within the MyDirectives software, and most (94%) of the sample wanted their physicians to consult a supportive and palliative care team, an option not typically available in most ADs. Close to 85% of respondents preferred stopping all life-sustaining treatments during their final days, 76% preferred to spend their final days at home or in a hospice facility, and only about 3% preferred to die in a hospital. There was no significant difference between men and women in this dimension.

Fifteen percent of respondents preferred one of several other options not typically available on most ADs. Of those who wanted to “keep trying life-sustaining treatment” at that stage, over 70% preferred to let their healthcare agent decide how long to keep trying. Within this group, women (76.7%) were more likely than men (60.7%) to defer decisions to their healthcare agent.

Among the respondents, 70% wanted CPR attempted unless their physician indicated they were terminal, they had a serious brain injury, CPR would do more harm than good, or CPR would not work. In contrast, 8% did not want CPR attempted in any circumstance, and 5% wanted CPR attempted in all circumstances, and these were often the same persons who wanted to maintain intensive treatment in the face of terminal illness. Only 15% preferred to rely on a healthcare agent to decide. No significant gender difference was detected for these decisions.

Most respondents indicated they would want an autopsy under the following conditions: 1) their physicians thought it would help others (31.3%), 2) there were questions about their death (28.2%), or 3) the person who was designated by law decided to do so (19.3%) (Table 1). Finally, 62% of the respondents indicated that they would like to donate their organs.

We also examined participants’ responses to the question “What is important to you?” As shown in Table 2, quality of
Table 1. Responses from a sample of 900 US individuals on the main questions in the online advanced directives

<table>
<thead>
<tr>
<th>Life-sustaining treatments</th>
<th>Combined</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stop all life-sustaining treatments</td>
<td>759 (84.3%)</td>
<td>353 (86.7%)</td>
<td>406 (82.4%)</td>
</tr>
<tr>
<td>Keep trying life-sustaining treatments…</td>
<td>71 (7.9%)</td>
<td>28 (6.9%)</td>
<td>43 (8.7%)</td>
</tr>
<tr>
<td>For selected period</td>
<td>9 (12.7%)</td>
<td>7 (25.0%)</td>
<td>2 (4.7%)</td>
</tr>
<tr>
<td>Indefinitely</td>
<td>12 (16.9%)</td>
<td>4 (14.3%)</td>
<td>8 (18.6%)</td>
</tr>
<tr>
<td>Let healthcare agent decide</td>
<td>50 (70.4%)</td>
<td>17 (60.7%)</td>
<td>33 (76.7%)</td>
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<tr>
<td>Neither of the options works for me</td>
<td>70 (7.8%)</td>
<td>26 (6.4%)</td>
<td>44 (8.9%)</td>
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<table>
<thead>
<tr>
<th>Cardiopulmonary resuscitation (CPR)</th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Want CPR attempted with limitations</td>
<td>629 (69.9%)</td>
<td>288 (70.7%)</td>
<td>339 (68.8%)</td>
</tr>
<tr>
<td>Do not want CPR in any circumstance</td>
<td>76 (8.4%)</td>
<td>37 (9.1%)</td>
<td>40 (8.1%)</td>
</tr>
<tr>
<td>Let healthcare agent decide</td>
<td>150 (16.7%)</td>
<td>60 (14.7%)</td>
<td>90 (18.3%)</td>
</tr>
<tr>
<td>Want CPR attempted in all circumstances</td>
<td>44 (4.9%)</td>
<td>21 (5.2%)</td>
<td>24 (4.9%)</td>
</tr>
<tr>
<td>Not sure</td>
<td>1 (0.1%)</td>
<td>1 (0.3%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Consulting a supportive and palliative care team</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>846 (94.0%)</td>
<td>371 (91.2%)</td>
<td>475 (96.4%)</td>
</tr>
<tr>
<td>No</td>
<td>54 (6.0%)</td>
<td>36 (8.9%)</td>
<td>18 (3.7%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Where to spend the final days</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>At home</td>
<td>574 (63.8%)</td>
<td>276 (67.8%)</td>
<td>298 (60.5%)</td>
</tr>
<tr>
<td>Hospice care at home</td>
<td>486 (84.7%)</td>
<td>228 (82.6%)</td>
<td>258 (86.6%)</td>
</tr>
<tr>
<td>In the hospital</td>
<td>29 (3.2%)</td>
<td>14 (3.4%)</td>
<td>15 (3.0%)</td>
</tr>
<tr>
<td>Consultation with a palliative care team</td>
<td>21 (72.4%)</td>
<td>11 (78.6%)</td>
<td>10 (66.7%)</td>
</tr>
<tr>
<td>In a hospice facility</td>
<td>116 (12.9%)</td>
<td>45 (11.1%)</td>
<td>71 (14.4%)</td>
</tr>
<tr>
<td>Not sure</td>
<td>181 (20.1%)</td>
<td>72 (17.7%)</td>
<td>109 (22.1%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Autopsy</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Want an autopsy if my doctor thinks it will help others</td>
<td>282 (31.3%)</td>
<td>134 (32.9%)</td>
<td>148 (30.0%)</td>
</tr>
<tr>
<td>Want an autopsy only if there are questions about my death</td>
<td>254 (28.2%)</td>
<td>104 (25.6%)</td>
<td>150 (30.4%)</td>
</tr>
<tr>
<td>Do not want an autopsy</td>
<td>147 (16.3%)</td>
<td>69 (17.0%)</td>
<td>78 (15.8%)</td>
</tr>
<tr>
<td>Want the person who’s designated by law to make this decision to decide after I die</td>
<td>174 (19.3%)</td>
<td>84 (20.6%)</td>
<td>90 (15.3%)</td>
</tr>
<tr>
<td>Not sure</td>
<td>43 (4.8%)</td>
<td>16 (3.9%)</td>
<td>27 (5.5%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Organ and tissue donations</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Donate organs</td>
<td>554 (61.6%)</td>
<td>247 (60.7%)</td>
<td>307 (62.3%)</td>
</tr>
<tr>
<td>Do not donate</td>
<td>346 (38.4%)</td>
<td>160 (39.3%)</td>
<td>186 (37.7%)</td>
</tr>
</tbody>
</table>

life was the most important concern for the last stage of life (e.g., avoiding prolonged dependence on machines, 85.3%; being free of pain, 84.2%; avoiding prolonged dependence on artificial or assisted nutrition through tubes, 78.4%). Another important factor was not being a burden to family, either financially (79.3%) or physically (79.2%). About 75% preferred to be with family in the last days of life.

About 12% of people changed their ADs at least once (with a range of 1 to 4 changes). Most of these changes (75%) were made more than 1 day after the initial AD creation, with about 30% of changes made more than 4 months after AD creation.

DISCUSSION

The MyDirectives data suggest that online AD platforms can help individuals from a wide range of ages and conditions engage in an interrogatory process about values and then develop an AD reflecting those values. According to Rao et al, AD completion among US adults is associated with older age and an increased likelihood of having a chronic disease (4). This early experience data set from MyDirectives suggests that an online approach can encourage younger people to participate in ACP earlier than society would normally engage them; in addition, the approach corrects the misconceptions that ADs are only relevant to the old and sick and that the elderly can’t use the Internet. The emotional harm to patients and their families occurring when young persons have an unexpected and sudden irreversible health event leaving them unable to communicate—as occurred with Quinlan, Cruzan, and Schiavo—serves as a reminder of the importance of ACP at a younger age than is typical under current practice.

Many patients, families, and healthcare professionals erroneously believe that a living will is meant only to limit life-sustaining treatment, and most state living will forms allow only that preference. However, truly patient-centered ADs must allow a preference for intensive and/or prolonged treatment in terminal or irreversible illness. Our data suggest that while most participants preferred cessation of life-sustaining treatment if terminally ill, 16% preferred a more nuanced approach, including 1.2% who preferred indefinite, unlimited treatment in the setting of terminal illness.

One advantage of a digital ACP tool is its ability to ask novel questions and offer definitions, video tutorials, and links to additional information. Such additional information about palliative medicine may help explain the 94% preference rate for palliative care consultation, a relatively new concept in medical care. This result is consistent with findings from the Center to Advance Palliative Care, which noted that when patients understand what palliative medicine is, they want to receive it when needed (23).

The autopsy question is another novel aspect of this ACP platform. Despite the benefits of autopsy (24, 25), nonforensic...
autopsy rates are around 5% (26). The reasons for the low percentage are multiple, but at least one is physician attitude and discomfort in asking for an autopsy (27). This discomfort may be unfounded because <17% would not want an autopsy. If these data hold true in a larger future sample size, perhaps physicians will be more willing to request an autopsy, especially when they see it as part of the patient’s AD.

Finally, nearly 124,000 persons are awaiting organ transplant in the United States (28), and as of 2012, 42.7% of the US population was a registered organ and/or tissue donor. The percentage of those using this online ACP/AD platform wishing to be donors was nearly 50% higher. Reasons are unclear, but we speculate that contemplating one’s own death increases the percentage are multiple, but at least one is physician attitude and discomfort in asking for an autopsy (27). This discomfort may be unfounded because <17% would not want an autopsy. If these data hold true in a larger future sample size, perhaps physicians will be more willing to request an autopsy, especially when they see it as part of the patient’s AD.

Table 2. Responses from a sample of 900 US individuals on issues important to them in advance care planning

<table>
<thead>
<tr>
<th>Issue</th>
<th>Combined</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoiding prolonged dependence on machines</td>
<td>768 (85.3%)</td>
<td>334 (82.1%)</td>
<td>434 (88.0%)</td>
</tr>
<tr>
<td>Being free from pain</td>
<td>758 (84.2%)</td>
<td>332 (81.6%)</td>
<td>426 (86.4%)</td>
</tr>
<tr>
<td>Not being a financial burden to my family</td>
<td>714 (79.3%)</td>
<td>316 (77.6%)</td>
<td>398 (80.7%)</td>
</tr>
<tr>
<td>Not being a physical burden to my family</td>
<td>713 (79.2%)</td>
<td>320 (78.6%)</td>
<td>393 (79.7%)</td>
</tr>
<tr>
<td>Avoiding prolonged dependence on artificial or assisted nutrition</td>
<td>706 (78.4%)</td>
<td>313 (76.9%)</td>
<td>393 (79.7%)</td>
</tr>
<tr>
<td>Being with my family</td>
<td>670 (74.4%)</td>
<td>282 (69.3%)</td>
<td>388 (78.7%)</td>
</tr>
<tr>
<td>Being able to feed, bathe, and take care of myself</td>
<td>610 (67.8%)</td>
<td>275 (67.6%)</td>
<td>335 (68.0%)</td>
</tr>
<tr>
<td>Being at peace with my God</td>
<td>332 (36.9%)</td>
<td>128 (31.5%)</td>
<td>204 (41.4%)</td>
</tr>
<tr>
<td>Dying at home</td>
<td>307 (34.1%)</td>
<td>130 (31.9%)</td>
<td>177 (35.9%)</td>
</tr>
<tr>
<td>Resolving conflicts</td>
<td>194 (21.6%)</td>
<td>81 (19.9%)</td>
<td>113 (22.9%)</td>
</tr>
<tr>
<td>Other things that are very important to me about life and health</td>
<td>106 (11.8%)</td>
<td>37 (9.1%)</td>
<td>69 (14.0%)</td>
</tr>
</tbody>
</table>

In conclusion, early experience with this digital ACP platform indicates that individuals acting on their own can complete an AD more nuanced than the typical paper-based directive. The ability and motivation of the patient/consumer to create a digital AD online is further supported by our recent research demonstrating that some people consider end-of-life issues too personal to discuss with a nonfamily member such as a physician (30). This early experience with digital ACP demonstrates that the reengineering of ACP suggested by Chiarighiaro and others is already happening. It is time to further expand the model.

Nationally, health care providers wrote 259 million prescriptions for narcotic analgesics in 2012, or roughly one bottle of narcotics per US adult (1). In an effort to combat this ever-growing problem, the Drug Enforcement Administration changed the schedule of hydrocodone combination products from schedule III to schedule II on October 6, 2014. Fourteen Baylor Scott & White pharmacies encompassing a 200-mile radius in Central Texas were queried for prescription information on hydrocodone/acetaminophen, morphine, codeine/acetaminophen, and tramadol before and after the rescheduling to evaluate trends in prescription drug usage. While the rescheduling of hydrocodone combination products resulted in a reduced number of prescriptions and the total quantity dispensed of both the hydrocodone/acetaminophen 5/325 mg (Norco 5/325) and 10/325 mg (Norco 10/325) formulations, this was offset by a dramatic increase in alternative narcotic analgesics such as tramadol, codeine/acetaminophen 30/300 mg (Tylenol #3), and codeine/acetaminophen 60/300 mg (Tylenol #4), which do not have schedule II requirements. Additionally, there was no significant reduction in total pain medication prescribed after converting all agents to morphine equivalents.

In 2011, the Centers for Disease Control and Prevention declared overdose from prescription narcotics to be an epidemic in the United States (1). In an attempt to reduce misuse, the Drug Enforcement Administration changed the schedule of hydrocodone combination products from schedule III to schedule II on October 6, 2014, resulting in significant changes in the prescribing, handling, and distribution of these drugs. Currently, there are at least 93 formulations of hydrocodone in combination with acetaminophen or ibuprofen marketed as either analgesics or cough suppressants in the United States. Of these combinations, hydrocodone/acetaminophen products are by far the most popular formulation and were the most frequently prescribed drug from 2007 to 2011 (1). Despite the almost universal acknowledgment of the growing prescription drug abuse epidemic in the US, many health care providers worried that changing hydrocodone combination products would only result in increased administrative tasks without a substantial decrease in overall opiate abuse and overdose (2). Our study hypothesized that rescheduling of hydrocodone combination products would lead to a decrease in prescriptions for hydrocodone combination products; however, this would be offset by increases in other schedule III narcotic prescriptions such as tramadol and codeine/acetaminophen formulations.

METHODS

Fourteen Baylor Scott & White pharmacies encompassing a 200-mile radius in Central Texas were queried for narcotic prescription information from July 2014 through January 2015. Our study focused on the most commonly prescribed hydrocodone combination products, namely the hydrocodone/acetaminophen 5/325 mg (Norco 5/325) and 10/325 mg (Norco 10/325) formulations. We also obtained prescription information on several schedule III narcotic medications, including tramadol, codeine/acetaminophen 30/300 mg (Tylenol #3), and codeine/acetaminophen 60/300 mg (Tylenol #4). Prescription information on oral morphine sulfate was obtained as a control.

Pharmaceutical data from July 2014 through September 2014 before the rescheduling were then compared to data from November 2014 through January 2015 after rescheduling to evaluate trends in prescription drug usage. Statistical analysis using the Poisson test of means was used to compare the number of prescriptions as well as the quantity of medication dispensed between these time periods. This test was done for each of the individual medications as well as the overall total. Statistical significance was indicated by a Pvalue < 0.05. Each medication was then converted to its morphine equivalent, and the total quantity of morphine equivalents dispensed in the 3-month period before the rescheduling was compared to that in the 3-month period after rescheduling.

RESULTS

Statistical analysis of the number of prescriptions received for each medication illustrated a 17% increase in tramadol, 597% increase in Tylenol #3, and 1056% increase in Tylenol #4 after federal rescheduling of hydrocodone combination products. In contrast, there was a 58% reduction in Norco 5/325,

From the Departments of Medicine (Seago, Newman), Pulmonary and Critical Care (Hayek), and Biostatistics (Pruszynski), Scott & White Memorial Hospital, Baylor Scott & White Health, Temple, Texas; and Texas A&M Health Sciences Center College of Medicine, Temple, Texas (Newman).

Corresponding author: Susan Seago, MD, Baylor Scott & White Health, 2401 S. 31st Street, Temple, TX 76508 (e-mail: sseago@sw.org)
34% reduction in Norco 10/325, and no statistically significant change in morphine sulfate (Table 1).

Further review of the quantity of medications dispensed illustrated a 42% reduction in the quantity of dispensed Norco 5/325, 14% reduction in Norco 10/325, and 7% reduction in oral morphine sulfate after federal rescheduling. During the same period, however, there was a 9% increase in tramadol, 122% increase in Tylenol #3, and 828% increase in Tylenol #4, resulting in a very modest 6% net decrease in total quantity of narcotic medications filled (Table 2 and Figure 1). Additionally, when all narcotic prescriptions were converted to morphine equivalents, there was only a small

Table 1. Number of prescriptions for each medication before and after federal rescheduling of hydrocodone combination products

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total before</th>
<th>Rate before (/month)</th>
<th>Total after</th>
<th>Rate after (/month)</th>
<th>Rate ratio</th>
<th>% change</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol</td>
<td>4463</td>
<td>1488</td>
<td>5199</td>
<td>1733</td>
<td>1.17</td>
<td>17%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tylenol #3</td>
<td>278</td>
<td>93</td>
<td>1938</td>
<td>646</td>
<td>6.97</td>
<td>+597%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tylenol #4</td>
<td>32</td>
<td>11</td>
<td>370</td>
<td>124</td>
<td>11.56</td>
<td>+1056%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Norco 5/325</td>
<td>4708</td>
<td>1570</td>
<td>1976</td>
<td>659</td>
<td>0.42</td>
<td>-58%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Norco 10/325</td>
<td>6260</td>
<td>2087</td>
<td>4128</td>
<td>1376</td>
<td>0.66</td>
<td>-34%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Morphine sulf</td>
<td>528</td>
<td>176</td>
<td>520</td>
<td>174</td>
<td>0.98</td>
<td>-2%</td>
<td>0.8288</td>
</tr>
<tr>
<td>Total</td>
<td>16,269</td>
<td>5423</td>
<td>14,131</td>
<td>4711</td>
<td>0.87</td>
<td>-13%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 2. Quantity of pills dispensed for each medication before and after federal rescheduling of hydrocodone combination products

<table>
<thead>
<tr>
<th>Drug</th>
<th>Total before</th>
<th>Rate before (/month)</th>
<th>Total after</th>
<th>Rate after (/month)</th>
<th>Rate ratio</th>
<th>% change</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tramadol</td>
<td>347,368</td>
<td>115,790</td>
<td>379,658</td>
<td>126,553</td>
<td>1.09</td>
<td>+9%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tylenol #3</td>
<td>39,913</td>
<td>11,305</td>
<td>88,458</td>
<td>29,486</td>
<td>2.22</td>
<td>+122%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tylenol #4</td>
<td>2,639</td>
<td>880</td>
<td>24,486</td>
<td>8,162</td>
<td>9.28</td>
<td>+828%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Norco 5/325</td>
<td>243,292</td>
<td>81,098</td>
<td>141,221</td>
<td>47,044</td>
<td>0.58</td>
<td>-42%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Norco 10/325</td>
<td>534,505</td>
<td>178,169</td>
<td>459,933</td>
<td>153,311</td>
<td>0.86</td>
<td>-14%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Morphine sulf</td>
<td>51,260</td>
<td>17,087</td>
<td>47,676</td>
<td>15,892</td>
<td>0.93</td>
<td>-7%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total</td>
<td>1,218,977</td>
<td>406,326</td>
<td>1,141,432</td>
<td>380,478</td>
<td>0.94</td>
<td>-6%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

DISCUSSION

While the rescheduling of hydrocodone combination products resulted in a reduced number of prescriptions for both the Norco 5/325 and Norco 10/325 formulations, this was offset by a dramatic increase in schedule III narcotic analgesics including tramadol, Tylenol #3, and Tylenol #4. With the significant rise in alternative prescriptions, there was only a slight change in the quantity of morphine equivalents prescribed before and after the federal rescheduling. Although schedule III medications are considered to have a lower potential for abuse than schedule II medications, many health care providers are less familiar with these medications and are therefore less equipped to handle potential side effects. Additionally, multiple studies have demonstrated an extreme variance in tramadol’s effectiveness and side effects within the general population, with ultra-rapid CYP2D6 enzyme metabolizers having increased toxicity and slow CYP2D6 enzyme metabolizers having fewer analgesic effects (3).

Our study illustrates an important and evolving trend in narcotic prescription habits after federal rescheduling of hydrocodone combination products and highlights the need for further research on effective means for controlling prescription drug abuse in the United States. A recently released study demonstrated a modest decrease in opioid prescriptions following the initiation of Florida’s Prescription Drug Monitoring Program, or so-called “pill mill laws.” Rather than increase legislation on specific medications, this legislation focused primarily on clinics with the highest rates of narcotic prescriptions per month. The new legislation required these clinics to register
with the state, have a physician owner, and maintain an electronic, statewide database (4). Additionally, the Food and Drug Administration (FDA) introduced a number of other initiatives to discourage opioid abuse, including voluntary educational programs for providers on how to recognize abuse, funding for abuse-deterrent narcotic formulations, and packaging and labeling changes on current narcotic formulations (5).

Though prescription drug abuse is an undeniable problem in the United States, this study demonstrates several shortcomings of the federal rescheduling of hydrocodone combination products. While several other state and FDA regulations show promise, there is little published data regarding the effectiveness of specific drug policies (4). With approximately 44 deaths due to prescription drug overdose each day, increased research and a multifaceted approach are essential in combating the prescription drug abuse epidemic.


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**In memoriam**

**CHARLES T. RICHARDSON, MD**  
*Division of Gastroenterology, Baylor University Medical Center at Dallas*

Charles T. Richardson, MD, died on February 1, 2016, at the age of 75. He grew up in Longview, Texas, and graduated from Baylor University and the University of Texas Southwestern Medical School. After completing his residency at Parkland Hospital and the Veterans Affairs Medical Center in Dallas, he practiced gastroenterology at Baylor University Medical Center at Dallas for many years, serving in the teaching program and on the Sammons Cancer Center Medical Committee, among other activities. In 1989, he formed a partnership with Dr. Charles Walker that would become Texas Digestive Disease Associates—a practice that now has more than 80 physicians. A fellow of the American College of Gastroenterology, Dr. Richardson had a long and respected career in academic medicine, where he received several grants and published numerous papers, as well as in private practice. Over the years he received numerous awards and was revered by his patients.
The impact of preexisting illness and substance use on functional and neuropsychological outcomes following traumatic brain injury

Marie N. Dahdah, PhD, Sunni A. Barnes, PhD, Amy Buros, MS, Andrew Allmon, BS, Rosemary Dubiel, DO, Cynthia Dunklin, BS, CCRC, Librada Callender, BS, CCRC, and Shahid Shafi, MD, MPH

Traumatic brain injury (TBI) is a significant public health problem in the US. Specific preexisting medical illnesses delay recovery after TBI and increase mortality or risk of repeat TBI. This study examined the impact of preexisting illness and substance use on patient rehabilitation outcomes following TBI. The Functional Independence Measure total score and Disability Rating Scale score measured functional outcomes at discharge from inpatient rehabilitation, while the Trail Making Test A and B and Total Trials 1-5 of the California Verbal Learning Test–II measured neuropsychological outcomes in 128 TBI survivors with moderate or severe TBI. Results showed that the presence of a heart condition or diabetes/high blood sugar was associated with lower functional outcomes by discharge. A history of a heart condition, stroke, or respiratory condition prior to TBI was associated with reduced cognitive flexibility. Those with preexisting diabetes/high blood sugar demonstrated poorer visual attention, visuomotor processing speed, and ability to learn and recall verbal information. Those with pre-TBI cancer also had greater auditory-verbal memory deficits. The findings showed that specific preexisting medical conditions are independently associated with lower functional and cognitive outcomes for patients with TBI. By screening patients for preexisting medical conditions, multidisciplinary TBI rehabilitation teams can identify patients who require more aggressive treatments or greater length of stay.

The purpose of this study was to examine the relation of preexisting medical illnesses and substance use with both functional status and neurocognitive status at the time of discharge from inpatient rehabilitation in individuals with traumatic brain injury (TBI). Preexisting cancer, preexisting liver disease, and use of tobacco/cigarettes were included, as few studies have examined their association with post-TBI functional outcomes. No studies to date have evaluated the impact of preexisting medical illnesses on neuropsychological outcomes.

METHODS

This study was part of the Traumatic Brain Injury Model System (TBIMS), with data collected at a center in an urban metroplex in the Southern US (1). TBIMS is a longitudinal multicenter, prospective, observational study of patients aged ≥16 years who sustained a moderate to severe TBI due to blunt or penetrating injuries. Additional information regarding TBIMS inclusion criteria and the definition of TBI can be found in Dijkers, Harrison-Felix, and Marwitz’s historical review of the TBIMS (1). Patients with concomitant spinal cord injury, whose inpatient rehabilitation course exceeded 90 days, or who died during their inpatient rehabilitation stay were excluded from this study. Collection of preexisting medical illnesses and substance use information was initiated in October 2012. Therefore, 138 patients enrolled in the TBIMS longitudinal study between October 1, 2012, and November 5, 2013, were screened for inclusion in this retrospective study. Of 138 screened patients, 128 (93%) had both complete functional outcome data and information regarding all preexisting health conditions in the TBIMS national database. Patients with preexisting medical illness (n = 39) were compared with those without any such illnesses (n = 89).

Of the 128 patients with preexisting health data, neuropsychological testing was obtained in 77 patients (60%) after repeated evaluation confirmed that the patients had emerged from posttraumatic amnesia (PTA) and were oriented 72 hours later during their rehabilitation course. The rest of the patients (n = 51) were still in PTA at or near the time of discharge from rehabilitation and hence were excluded from neuropsychological testing. Testing was completed by the neuropsychologist or psychometrist on the inpatient TBI service. Data were included
for analysis even if patients were outside the TBIMS testing window of 4 weeks (±2 weeks) postinjury (2). Despite the longitudinal nature of the TBIMS, only discharge outcomes were examined in this study, given that neuropsychological data were only collected during inpatient rehabilitation.

Based on preexisting health status and duration of PTA, patients fell into one of four groups: 1) patients with preexisting illness who completed neuropsychological measures; 2) patients with preexisting illness who did not complete neuropsychological measures; 3) patients without a history of preexisting illness who completed neuropsychological measures; and 4) patients without a history of preexisting illness who did not complete neuropsychological measures.

Functional outcomes were measured using the total score of the Functional Independence Measure (FIM) (3, 4) and Disability Rating Scale (DRS) (3, 5) at discharge. Neuropsychological outcomes were measured during inpatient rehabilitation using the Trail Making Test (TMT) (6–8) completion time in seconds and the California Verbal Learning Test, 2nd edition (CVLT-II) (9) total number of items immediately recalled on Trials 1 to 5. These are the only neuropsychological measures currently available in the TBIMS National Database.

Briefly, the FIM comprises 18 items designed to measure functional independence in self-care, mobility, and communication and social cognition (3, 4). Performance on each item is rated between 1 and 7 (7 = complete independence). The maximum score possible on the FIM is 126 (4). Higher FIM scores reflect better functional status. FIM efficiency was defined as FIM change (FIM discharge – FIM admission) divided by total length of stay, in days.

The DRS is an 8-item scale that incorporates a modification of the Glasgow Coma Scale items and other items assessing cognitive ability to manage activities of daily living, the need for assistance or supervision, and potential employability (3, 5). The maximum score possible on the DRS is 29, with zero indicating lack of disability. A lower DRS score reflects better functional status. DRS efficiency was defined as DRS change (DRS discharge – DRS admission) divided by total length of stay, in days.

The TMT consists of part A, which measures visual attention and visuomotor processing speed, and part B, which measures the same functions as part A and mental flexibility. It is a brief and reliable measure that has been shown to be sensitive to cognitive impairments commonly exhibited in individuals with TBI (6–8). The score is based on completion time in seconds for each part (TMT:A and TMT:B) and is converted to a T score.

The CVLT-II is a comprehensive assessment of auditory-verbal learning and memory. The split-half reliability estimate ranges between 0.90 and 0.96. Construct validity for the CVLT-II is adequate (9). A composite score reflecting total number of items learned and immediately recalled across five exposure trials (Total List A Trials 1–5) was used in this study and was presented in the form of a T score. This is the only CVLT-II index available in the TBIMS database.

Age, sex, race/ethnicity, years of education, marital status, duration of PTA, length of stay, discharge disposition (home vs. care facility), and functional status at admission using the FIM and DRS were included in the analysis (3, 10–16).

Information on the presence or absence of medical conditions and substance use prior to TBI was obtained from patients’ medical charts and by querying patients or family members. The conditions were predefined by the TBIMS: hypertension/high blood pressure, stroke, diabetes/high blood sugar/sugar in the urine, cancer, liver disease, emphysema/asthma/chronic obstructive pulmonary disease, use of tobacco/cigarettes, alcohol consumption, and use of illicit/nonprescription drugs. Congestive heart failure, myocardial infarction, and other heart conditions were merged into a single category, heart condition, due to the small number of patients in these individual heart conditions. Alcohol use was defined by the number of days per week or month alcoholic beverages (beer, wine, wine coolers, liquor) were consumed, the number of drinks consumed on average in a sitting, and the number of times the individuals consumed ≥5 drinks in a sitting the month prior to the TBI. Moderate use was 1 to 3 drinks and heavy use was >3 drinks, as defined by the National Institute on Alcohol Abuse and Alcoholism (17). Drug use was defined as use of any illicit or nonprescription drugs. This study was approved by Baylor University Medical Center’s institutional review board.

Analyses were conducted using SAS, version 9.3 (SAS Institute Inc., Cary, NC). Linear regression was used to measure associations between preexisting medical illness and patient outcomes, while adjusting for patient demographics, severity of TBI, and functional status at admission, with P < 0.05 considered significant. All assumptions justifying use of linear regression were satisfied. Separate models were developed for each of the five outcomes. First, regression analyses were conducted examining the relationship of an individual preexisting illness with five outcomes: FIM at discharge, DRS at discharge, TMT:A, TMT:B, and CVLT-II. Next, the full regression model was examined to evaluate the impact of all preexisting illnesses combined on the five outcomes. The full regression model included all of the preexisting medical illnesses and substance use as covariates, as well as other potential confounders listed previously. The GLMSelect procedure was used to find the optimal model using the Schwarz Bayesian criteria.

RESULTS

Table 1 summarizes patient demographics for each of the four groups. The mean age of the overall study population was 47 years. Approximately 75% were men, 28% were racial/ethnic minorities, and 32% were married. The education level of these patients varied from less than high school (11%) to completion of graduate school (12%). Fifty-nine percent of patients engaged in moderate or heavy alcohol use prior to the TBI. Patients were admitted to rehabilitation centers at a mean of 2 weeks after sustaining injuries and had a mean inpatient rehabilitation stay of 19 days. Patients emerged from PTA a mean of 2 weeks from the time of injury (range = 1 to 22 days). Nearly 88% of the patients were discharged to their homes. Table 2 shows patients’ functional status at admission and discharge and scores on three neuropsychological measures (TMT:A, TMT:B, and CVLT-II) during their inpatient stay.
Hypertension was the most common condition, found in 28% of patients (Table 3). About 16% had some form of heart condition, and about 10% had diabetes mellitus/high blood sugar. Few patients were diagnosed with stroke, respiratory conditions (emphysema/asthma/chronic obstructive pulmonary disease), cancer, or liver disease. Eighteen percent of the patients consumed >3 alcoholic beverages daily, while the rest consumed ≤3 alcoholic beverages daily (nonsignificant relationship with outcomes and therefore alcohol consumption was not included in Table 4). About 13% used illicit substances and 34% used tobacco or nicotine before their injury, but these predictors were not associated with outcomes.

After adjusting for demographic variables, severity of TBI, and functional status at admission, regression analyses revealed that at discharge, patients with two or more of any type of preexisting medical illness performed a mean of 13 points lower on the FIM than patients without two or more illnesses. None of the preexisting illnesses alone demonstrated a significant relationship with any of the five outcomes (Table 4).

The full regression model (Table 5), which was also adjusted for demographic variables, severity of TBI, and functional status at admission, revealed that preexisting heart condition was associated with lower functional outcomes, as measured by

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**Table 1. Patient characteristics by group among 128 patients with traumatic brain injury**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Group 1 (n = 18)</th>
<th>Group 2 (n = 21)</th>
<th>Group 3 (n = 59)</th>
<th>Group 4 (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.4 ± 18.8</td>
<td>65.9 ± 20.0</td>
<td>39.4 ± 16.9</td>
<td>43.1 ± 19.1</td>
</tr>
<tr>
<td>Days from injury to rehab admission</td>
<td>10.9 ± 6.3</td>
<td>13.6 ± 7.5</td>
<td>14.4 ± 6.5</td>
<td>13.2 ± 7.0</td>
</tr>
<tr>
<td>Length of rehab stay (days)</td>
<td>19.3 ± 11.4</td>
<td>26.8 ± 18.4</td>
<td>19.1 ± 11.9</td>
<td>15.4 ± 15.3</td>
</tr>
<tr>
<td>Posttraumatic amnesia (days)</td>
<td>8.2 ± 11.9</td>
<td>17.8 ± 22.2</td>
<td>13.7 ± 11.4</td>
<td>17.3 ± 17.9</td>
</tr>
<tr>
<td>Discharge to home</td>
<td>83.3% (15)</td>
<td>71.4% (15)</td>
<td>88.8% (53)</td>
<td>96.7% (29)</td>
</tr>
<tr>
<td>Gender: Male</td>
<td>66.7% (12)</td>
<td>52.4% (11)</td>
<td>78.0% (46)</td>
<td>90% (27)</td>
</tr>
<tr>
<td>Racial/ethnic minority</td>
<td>38.9% (7)</td>
<td>23.8% (5)</td>
<td>22.0% (13)</td>
<td>36.7% (11)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>16.7% (3)</td>
<td>14.3% (3)</td>
<td>15.3% (9)</td>
<td>23.3% (7)</td>
</tr>
<tr>
<td>Education</td>
<td>16.1% (15)</td>
<td>52.4% (11)</td>
<td>25.4% (15)</td>
<td>33.3% (10)</td>
</tr>
</tbody>
</table>

Group 1 indicates patients with preexisting illness who completed neuropsychological measures; Group 2, patients with preexisting illness who did not complete neuropsychological measures; Group 3, patients with no preexisting illness who completed neuropsychological measures; Group 4, patients with no preexisting illness who did not complete neuropsychological measures.

---

**Table 2. Functional and neuropsychological measurements (outcome variables) in patients with and without preexisting illnesses before traumatic brain injury**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group 1 (n = 18)</th>
<th>Group 2 (n = 21)</th>
<th>Group 3 (n = 59)</th>
<th>Group 4 (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIM at admission</td>
<td>54.8 ± 18.2</td>
<td>65.9 ± 20.0</td>
<td>39.4 ± 16.9</td>
<td>43.1 ± 19.1</td>
</tr>
<tr>
<td>FIM at discharge</td>
<td>89.2 ± 13.6</td>
<td>81.2 ± 95</td>
<td>80.9 ± 19.8</td>
<td>72 ± 94</td>
</tr>
<tr>
<td>DRS at admission</td>
<td>9.2 ± 3.1</td>
<td>7 ± 9</td>
<td>10.9 ± 4.5</td>
<td>8 ± 14</td>
</tr>
<tr>
<td>DRS at discharge</td>
<td>5.8 ± 1.7</td>
<td>5 ± 6</td>
<td>6.1 ± 2.9</td>
<td>5 ± 7</td>
</tr>
<tr>
<td>FIM efficiency*</td>
<td>2 ± 0.1</td>
<td>1.4 ± 2.6</td>
<td>1.6 ± 1.2</td>
<td>0.8 ± 1.9</td>
</tr>
<tr>
<td>DRS efficiency*</td>
<td>0.2 ± 0.1</td>
<td>0.1 ± 0.3</td>
<td>0.2 ± 0.2</td>
<td>0.1 ± 0.3</td>
</tr>
<tr>
<td>TMT Part A T score</td>
<td>30.1 ± 11.0</td>
<td>21 ± 37</td>
<td>–</td>
<td>23.2 ± 16.6</td>
</tr>
<tr>
<td>TMT Part B T score</td>
<td>27.5 ± 12.7</td>
<td>18.5 ± 39</td>
<td>–</td>
<td>32.4 ± 13.1</td>
</tr>
<tr>
<td>CVLT trials 1–5 T score</td>
<td>31.9 ± 14.5</td>
<td>19.5 ± 41</td>
<td>–</td>
<td>35.3 ± 18.7</td>
</tr>
</tbody>
</table>

*Efficiency is calculated as improvement.

CVLT indicates California Verbal Learning Test; DRS, Disability Rating Scale; FIM, Functional Independence Measure; Group 1, patients with preexisting illness who completed neuropsychological measures; Group 2, patients with preexisting illness who did not complete neuropsychological measures; Group 3, patients with no preexisting illness who completed neuropsychological measures; Group 4, patients with no preexisting illness who did not complete neuropsychological measures; IQR, interquartile range; SD, standard deviation; TMT, Trail Making Test.
Table 3. Preexisting medical conditions among 128 patients with traumatic brain injury

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart condition</td>
<td>20</td>
<td>15.6%</td>
</tr>
<tr>
<td>Hypertension/high blood pressure</td>
<td>35</td>
<td>28.0%</td>
</tr>
<tr>
<td>Stroke</td>
<td>6</td>
<td>4.8%</td>
</tr>
<tr>
<td>Diabetes/high blood sugar</td>
<td>12</td>
<td>9.5%</td>
</tr>
<tr>
<td>Cancer</td>
<td>5</td>
<td>4.0%</td>
</tr>
<tr>
<td>Liver disease</td>
<td>2</td>
<td>1.6%</td>
</tr>
<tr>
<td>Emphysema, asthma, COPD</td>
<td>8</td>
<td>6.4%</td>
</tr>
<tr>
<td>Alcohol consumed per sitting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3 drinks</td>
<td>21</td>
<td>18.0%</td>
</tr>
<tr>
<td>1–3 drinks</td>
<td>49</td>
<td>41.9%</td>
</tr>
<tr>
<td>None</td>
<td>47</td>
<td>40.1%</td>
</tr>
<tr>
<td>Illicit drug use</td>
<td>17</td>
<td>13.4%</td>
</tr>
<tr>
<td>Tobacco/cigarette use</td>
<td>35</td>
<td>34.4%</td>
</tr>
</tbody>
</table>

COPD indicates chronic obstructive pulmonary disease.

a 7.4-point lower discharge FIM score on average ($\beta = -7.37, P = 0.02$). Similarly, the presence of preexisting diabetes mellitus/high blood sugar was associated with a 12-point lower discharge FIM score ($\beta = -11.99, P = 0.003$).

Individuals with a history of a heart condition ($\beta = 87.98, P = 0.01$), stroke ($\beta = 57.56, P = 0.02$), or respiratory condition ($\beta = 159.36, P = 0.005$) demonstrated reduced cognitive flexibility. As an example, patients with a preexisting respiratory condition took 159 seconds longer on average to complete the TMT:B task (longer completion time on TMT:A and TMT:B equates to poorer performance). Patients with TBI who had preexisting diabetes/high blood sugar demonstrated poorer visual attention, visuomotor processing speed (TMT:A: $\beta = 25.25, P = 0.02$), and ability to learn and recall auditory-verbal information (CVLT-II: $\beta = -17.33, P = 0.005$). A history of cancer prior to TBI was associated with lower auditory-verbal learning and memory (CVLT-II: $\beta = -20.43, P = 0.01$). The final models explained varying magnitudes of variability in the outcomes (using $R^2$ for linear regression): FIM at discharge, 60%; DRS at discharge, 48%; TMT:A, 49%; TMT:B, 69%; and CVLT-II, 43%.

DISCUSSION

After accounting for demographic variables, severity of TBI, and functional status at admission, a history of a preexisting respiratory condition, cancer, and conditions known to be cerebrovascular risk factors (heart condition, stroke, diabetes/high blood sugar) remained significant predictors of functional outcomes and neurocognitive functioning at discharge from inpatient rehabilitation. In other words, worse outcomes were predicted beyond the direct effects of TBI.

The findings of this study relating to functional outcomes are similar to those in the study of Lew, Lee, and Zeiner, despite the fact that some different preexisting conditions and the DRS were additionally examined in the present study (18). Lew and his colleagues found that individuals with preexisting seizure disorder, congestive heart failure, diabetes mellitus, parkinsonism, and chronic low back pain obtained lower total FIM scores at admission and discharge from inpatient rehabilitation (18). These findings are relevant because half of TBI patients with preexisting medical conditions experience acute medical problems during their inpatient rehabilitation stay, which may further compromise gains (18).

Ensuring comprehensive medical treatment of these conditions early in TBI patients’ rehabilitation course may impact their functional outcomes. Medical interventions may vary from those previously prescribed to patients due to TBI-induced changes in pressure-volume dynamics that influence the relationship of blood pressure with intracranial pressure changes, and changes in oxygen, mineral, and water metabolism that can adversely affect renal, heart, and immune system functioning (19, 20).

Identification of these patients is also important because these risk factors are predictive of physical dependence and the potential of suffering a superimposed stroke/vascular event following the TBI (21). Cardiovascular risk factors (hypertension, coronary artery disease, diabetes mellitus, smoking, alcohol intake) have been shown to be associated with development of white matter lesions or small subcortical infarcts, which tend to be correlated with reduced premorbid cognition (21–26). Changes in executive function are most pronounced (21, 25). TBI is not currently identified as a risk factor for stroke. However, one trauma database found that 37% of trauma patients are admitted secondary to TBI and, in a 2½-year follow-up period, patients who suffered a TBI had a 31% increased risk of being hospitalized secondary to ischemic stroke over non-TBI trauma patients (27).

Since these specific preexisting conditions have the potential to alter the course of rehabilitation, an important implication is that patients with TBI should be screened for the presence of preexisting medical illness at the time of admission to inpatient rehabilitation. Knowledge of a preexisting respiratory condition will allow rehabilitation care teams to better personalize that patient’s care by prompting ancillary referrals. Augmentation of care via aggressive respiratory therapy may enable these patients to make functional gains that would be delayed or lost due to oxygen insufficiency. Receiving information regarding a preexisting history of diabetes/high blood sugar sooner can facilitate immediate placement of a patient on an American Diabetes Association–approved diet. Family members can be trained to routinely check the patient’s blood glucose levels and offer snacks depending on their readings, or a glycosylated hemoglobin test can be initiated for cognitively impaired individuals. Additional treatment/therapies for heart or respiratory problems may extend length of stay beyond what is indicated by the patient’s payer. This information may play a role in TBI advocacy efforts and may indicate a need for follow-up care following discharge from inpatient rehabilitation.

Evidence that a subset of individuals with TBI experience progressive functional decline in the years following TBI may
explain why researchers in TBI and the Institute of Medicine are beginning to consider TBI a chronic health condition (28, 29). These findings highlight a need to study any reversible risk factors that may be associated with further cognitive deterioration in patients with TBI and additional medical illnesses that may develop in the months and years following discharge from inpatient rehabilitation. Early identification and treatment of medical conditions is an important part of TBI rehabilitation. Beginning to consider TBI a chronic health condition (28, 29) explains why researchers in TBI and the Institute of Medicine are beginning to consider TBI a chronic health condition (28, 29). These findings highlight a need to study any reversible risk factors that may be associated with further cognitive deterioration in patients with TBI and additional medical illnesses that may develop in the months and years following discharge from inpatient rehabilitation. Early identification and treatment of medical conditions is an important part of TBI rehabilitation care.

The results should be interpreted in light of the study’s limitations. This study involved a small sample size, and neuropsychological test data were available for only about half of the patients. Selection of neuropsychological outcome measures was limited by availability of specific measures and indices in the TBIMS national database. Data entry of one specific CVLT-II index is required of TBIMS centers. A future study examining the relationship between preexisting conditions and other indices of the CVLT-II that measure executive functioning and additional executive measures assessing word generation, problem-solving, and inhibition would be beneficial. Only discharge outcomes were examined, given that neuropsychological variables are collected during inpatient rehabilitation but not at follow-up intervals.

No data were available concerning services received by patients during inpatient rehabilitation and the amount of time spent in each rehabilitation discipline. Therefore, the impact of receiving speech, physical, and occupational therapies on outcomes in this study is not known. This was a single TBIMS center study, and hence the findings may not be generalizable to other rehabilitation centers or to the entire population of individuals with TBI. Patient functional outcome measurements varied by the tool used despite moderate correlations between the DRS and FIM (r = −0.58). As noted in a previous study by these authors, this highlights the need for a composite score using multiple existing tools to measure functional outcomes (30). Inclusion of predictors was not exhaustive, and variables such as family support and income were not available but may have influenced the strength of the relationship between preexisting medical illness and outcomes in this study.

The specific preexisting conditions included as predictors were those that were available in the database. Had preexisting conditions such as seizure disorder/epilepsy and pain been available, they could have been included in the analyses as well. Information regarding preexisting psychological illnesses was also unavailable, but it would be interesting to examine their impact on functional and neurocognitive outcomes as well. This study was further limited by a lack of information regarding subtypes and anatomic location of the diseases. It was unknown whether a patient was diagnosed with a brain malignancy versus colon cancer or whether a patient had type 1 versus type 2 diabetes. It was unknown if preexisting conditions were controlled or uncontrolled at the time of injury or were severe, chronic, or reversible.

Table 4. Regression analyses of individual preexisting conditions associated with functional and neuropsychological outcomes among 128 patients with traumatic brain injury

<table>
<thead>
<tr>
<th>Preexisting condition</th>
<th>Mean (SD)</th>
<th>FIM total at discharge</th>
<th>DRS at discharge</th>
<th>TMT Part A T score</th>
<th>TMT Part B T score</th>
<th>CVLT trials 1-5 T score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes/high blood sugar</td>
<td>Present</td>
<td>83.6 (22.5)</td>
<td>5.8 (1.8)</td>
<td>31.7 (9.0)</td>
<td>32.8 (16.6)</td>
<td>30.8 (9.2)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>95.0 (16.0)</td>
<td>5.5 (2.0)</td>
<td>31.6 (15.9)</td>
<td>31.1 (13.1)</td>
<td>34.6 (18.3)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.095</td>
<td>0.65</td>
<td>0.15</td>
<td>0.29</td>
<td>0.96</td>
</tr>
<tr>
<td>Heart condition</td>
<td>Present</td>
<td>86.6 (15.5)</td>
<td>6.0 (2.8)</td>
<td>33.9 (10.5)</td>
<td>32.4 (8.3)</td>
<td>35.5 (16.0)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>95.2 (16.8)</td>
<td>5.4 (1.7)</td>
<td>31.4 (15.9)</td>
<td>31.1 (13.6)</td>
<td>34.5 (18.1)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.13</td>
<td>0.55</td>
<td>0.48</td>
<td>0.79</td>
<td>0.70</td>
</tr>
<tr>
<td>Emphysema, asthma, COPD</td>
<td>Present</td>
<td>85.4 (11.1)</td>
<td>5.8 (1.5)</td>
<td>29.5 (12.0)</td>
<td>21.0 (12.7)</td>
<td>42.0 (35.4)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>94.4 (17.3)</td>
<td>5.5 (2.0)</td>
<td>31.6 (15.7)</td>
<td>31.4 (13.2)</td>
<td>33.8 (17.4)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.24</td>
<td>0.59</td>
<td>0.25</td>
<td>0.36</td>
<td>0.66</td>
</tr>
<tr>
<td>Cancer</td>
<td>Present</td>
<td>78.4 (12.1)</td>
<td>6.8 (2.4)</td>
<td>26.0 (15.8)</td>
<td>23.5 (17.6)</td>
<td>22.0 (7.9)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>94.5 (16.9)</td>
<td>5.4 (1.9)</td>
<td>31.9 (15.4)</td>
<td>31.7 (12.9)</td>
<td>34.8 (17.9)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.55</td>
<td>0.50</td>
<td>0.07</td>
<td>0.49</td>
<td>0.37</td>
</tr>
<tr>
<td>Stroke</td>
<td>Present</td>
<td>86.0 (19.6)</td>
<td>6.5 (2.2)</td>
<td>27.6 (9.0)</td>
<td>19.0 (12.8)</td>
<td>33.0 (17.5)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>94.2 (16.9)</td>
<td>5.5 (1.9)</td>
<td>31.9 (15.9)</td>
<td>32.1 (12.9)</td>
<td>34.1 (17.9)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.40</td>
<td>0.35</td>
<td>0.87</td>
<td>0.63</td>
<td>0.10</td>
</tr>
<tr>
<td>Liver disease</td>
<td>Present</td>
<td>94.5 (0.7)</td>
<td>5.0 (0)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>93.8 (17.2)</td>
<td>5.5 (1.9)</td>
<td>31.6 (15.5)</td>
<td>31.1 (13.2)</td>
<td>34.0 (17.7)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.65</td>
<td>0.46</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Hypertension/high blood pressure</td>
<td>Yes</td>
<td>92.5 (21.8)</td>
<td>5.6 (2.2)</td>
<td>31.6 (15.0)</td>
<td>34.6 (16.9)</td>
<td>27.5 (13.5)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>94.3 (14.8)</td>
<td>5.5 (1.8)</td>
<td>34.9 (14.8)</td>
<td>30.4 (15.0)</td>
<td>32.3 (13.1)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.34</td>
<td>0.47</td>
<td>0.07</td>
<td>0.80</td>
<td>0.09</td>
</tr>
<tr>
<td>Any condition</td>
<td>Present</td>
<td>84.7 (17.5)</td>
<td>6.0 (2.4)</td>
<td>30.1 (11.0)</td>
<td>27.5 (12.7)</td>
<td>31.9 (14.5)</td>
</tr>
<tr>
<td></td>
<td>Absent</td>
<td>97.9 (14.9)</td>
<td>5.2 (1.7)</td>
<td>32.3 (16.6)</td>
<td>32.4 (13.1)</td>
<td>35.3 (18.7)</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>0.02</td>
<td>0.66</td>
<td>0.09</td>
<td>0.31</td>
<td>0.62</td>
</tr>
</tbody>
</table>

COPD indicates chronic obstructive pulmonary disease; CVLT, California Verbal Learning Test; DRS, Disability Rating Scale; FIM, Functional Independence Measure; TMT, Trail Making Test.
### Table 5. Multivariate regression analyses of preexisting conditions associated with higher or lower functional and neuropsychological outcomes

<table>
<thead>
<tr>
<th>Predictors</th>
<th>FIM DC</th>
<th>DRS DC</th>
<th>TMT:A</th>
<th>TMT:B</th>
<th>CVLT-II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart condition</td>
<td>10.37</td>
<td>0.02</td>
<td>5.57</td>
<td>0.15</td>
<td>5.20</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5.30</td>
<td>0.07</td>
<td>5.96</td>
<td>0.14</td>
<td>7.20</td>
</tr>
<tr>
<td>Stroke</td>
<td>5.07</td>
<td>0.15</td>
<td>5.67</td>
<td>0.12</td>
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<tr>
<td>Diabetes/high blood sugar</td>
<td>11.99</td>
<td>0.003</td>
<td>25.25</td>
<td>0.02</td>
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<tr>
<td>Cancer</td>
<td>10.87</td>
<td>0.15</td>
<td>1.57</td>
<td>0.92</td>
<td>9.55</td>
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<tr>
<td>Liver</td>
<td>1.62</td>
<td>0.87</td>
<td>1.57</td>
<td>0.90</td>
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<tr>
<td>Emphysema/asthma/COCPD</td>
<td>15.41</td>
<td>0.14</td>
<td>1.52</td>
<td>0.72</td>
<td>159.36</td>
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<td>1–3 alcoholic drinks</td>
<td>0.76</td>
<td>0.02</td>
<td>5.68</td>
<td>0.62</td>
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<tr>
<td>&gt;3 alcoholic drinks</td>
<td>0.11</td>
<td>0.66</td>
<td>2.78</td>
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<td>48.54</td>
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<td>Illicit drug use</td>
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<td>0.28</td>
<td>0.60</td>
<td>0.95</td>
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<tr>
<td>Tobacco/cigarette use</td>
<td>0.14</td>
<td>0.64</td>
<td>0.72</td>
<td>0.93</td>
<td>19.95</td>
</tr>
</tbody>
</table>

*Significant: factor associated with lower outcomes. Note: There were no observations with both preexisting liver disease and neuropsychological outcomes.

COCPD indicates chronic obstructive pulmonary disease; DC, discharge; NS, outcomes not significant; CVLT-II, California Verbal Learning Test, 2nd edition; DRS, Disability Rating Scale; FIM, Functional Independence Measure; TMT, Trail Making Test.
Nursing preceptors initiate new staff to the professional environment. To be successful, preceptors must be willing and knowledgeable in their role, both clinically and as an instructor. This study evaluated the effects of a 4-hour preceptor class to change preceptor behavior. Twenty-seven class participants commented on the class and their goals, and 18 completed a follow-up survey 2 months later. Among those 18, 90% had achieved at least one of their goals. One barrier to achieving planned changes was having the opportunity to precept over the time period. Participants indicated that improved listening skills, application of content, and team building all supported their improvement as a preceptor.

Preceptors and preceptorships have been a part of nursing for many years. Preceptors teach students across a variety of acute, community, and continuing care practices (1). They provide a safety net of experienced staff to answer questions and provide insight (2). While there are multiple considerations for providing a preceptor experience, one study identified three themes associated with good preceptorships: a caring relationship, mutual respect, and a deep sense of responsibility (3).

Dusaj described the importance of the preceptor-preceptee relationship in ensuring a successful orientation (4). Specific actions of the preceptor include providing a tool box of resources and actions that prepare the new staff member to be successful. Preceptors also boost morale and confidence while making the new nurse feel a part of the team. Many authors depict preceptors as having the experience to guide new nurses as they assimilate into the new work environment. Galper stressed the importance of the preceptor having experience in the areas needed by the preceptee (5). In interviews with preceptors, Hilli et al concluded that a good preceptor has years of work experience, allowing a sense of security in the role of nurse (3). This is in line with the study of Chen, Li-Ling, and Suh-Ing, who identified the best preceptors as older, senior nurses who choose to precept (6). The preceptor-preceptee relationship not only guides and inspires new staff members, but introduces preceptors to ideas they may not have considered (7). Preceptors must be active teachers willing to share ideas and help new nurses search out answers, as well as excellent role models (8, 9).

Additionally, they must be able to manage poor performance and develop action plans when needed.

Preceptors face a broad set of teaching-learning diversity issues related to their role as clinical teachers. Being unaware of these issues may contribute to miscommunication and conflict. However, preceptors often have limited information on this diversity (8). The implication for nursing education is to prepare the preceptor for the role and thereby increase satisfaction and improve the preceptee’s experience. In a study by Kalischuck et al, preceptors expressed the need for a lighter workload, further educational preparation, and more time assessing and assisting students (1). They also felt a need for increased support of stakeholders. Increased support encourages preceptor retention and influences future nurses. The unprepared preceptor is not confident in the role (10). This lack of confidence could result in a poor transition of the preceptee to staff member, possibly increasing staff turnover and losing the new nurse to the profession. This retrospective study identified potential changes to the practice of nurse preceptors due to education and identified situations that facilitate or hinder such practice change.

METHODOLOGY

To facilitate preceptor development, three preceptor courses were provided in 2013. Each 4-hour class presented by a clinic educator covered the role of the preceptor, learning styles, growth and development of new staff, competency assessment, and critical thinking. Class participants were asked to identify three practice improvements based on course content. A total of 27 attendees identified anticipated changes in behavior due to participation in the preceptor class. Two months after the class, the students were asked to return the outcomes tool identifying which changes had occurred and to relate any barriers to making the changes. Eighteen tools were returned, for a 66% return rate: the January class had 15 attendees, and 13 responded at 2 months; the April class had 6 attendees, and 3 responded at 2 months; and the September class had 6 attendees, and 2 responded at 2 months.

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For the purposes of this paper, preceptor is defined as a nursing staff member—registered nurse, licensed vocational nurse, or certified medical assistant—who has attended a preceptor class and is charged with the orientation of a new staff member. The preceptor must have a job role equal to or higher than that of the preceptee. A preceptorship is defined as a relationship between an experienced nursing staff member and a newly hired staff member; the length of this relationship depends on the orientation period of the specific nursing unit or clinic.

RESULTS

Upon receiving institutional review board approval, the data were deidentified. The 27 participants were classified only as registered nurses (n = 8; 30%), licensed vocational nurses (n = 13; 48%), certified medical assistants (n = 3; 12%), and nonnursing staff (n = 3; 12%). The participants described long-term goals on the evaluation tool, listing the improvements or changes they planned to make as preceptors based on class learning. Narrative responses on the outcome measurement tool were categorized into three broad themes: 1) preceptor/teaching; 2) orientee/learning; and 3) role of the preceptor. Multiple goals identified by individual participants fell into more than one theme. Several participants commented on the learning from the class: “ensure my body language represents what I am really saying,” “teach new staff more about critical thinking and interpersonal skills because it isn’t all about technical skills,” and “appreciation that my body language represents what I am really saying.”

Eighteen participants (66%) completed the follow-up survey 2 months after the class. Of these, 16 (90%) achieved one or more of their goals. Of these 16, 3 (20%) achieved one goal, 5 (30%) achieved two goals, and 8 (50%) achieved three goals.

The respondents were asked to identify barriers to achieving their planned changes. One barrier was unexpected time away from the clinic so participants were not able to precept during the 2 months. Several stated they had not had the opportunity to practice the skills since no new nurses were hired. One comment was: “I have become generationally sensitive to my peers. The class was helpful in understanding my coworkers and their work ethic. I have not had to precept anyone thus far but will soon.”

When describing supportive factors to utilizing the content, three categories were identified: improved listening skills (n = 5), application of content (n = 8, including the ability to build on the preceptee’s strengths, generational sensitivity, and the creation of a resource manual), and team building (n = 6, including understanding coworkers and increased involvement). Examples of comments describing how the content was utilized in the work setting include:

• “After attending this class and learning about the different age groups/needs, training new employees has become easier and feel like I am able to reach them on their level due to the breakdown in age groups.”
• “I have been able to appreciate everyone’s role in the clinical setting. This in turn has helped me as a nurse contribute my strengths and abilities in a stronger way. Having recently had the opportunity to be ‘the preceptor’ to a young nurse, I was able to direct and be the person outlined in the class with more confidence and assurance.”
• “What facilitated the projected changes is the fact that I can be very open with coworkers and we work as a team. They also know they can be very open with me about any concerns.”

DISCUSSION

The results of this study suggest that the class was of value in enhancing the preceptor role by developing skills in the participants. Improvement of teaching was mentioned 27 times; this could indicate that basic nursing education does not ensure that staff nurses are ready to precept, and they need more preparation for this responsibility. The class also helped the preceptor realize that the learning needs of the preceptee may go beyond the technical aspects of nursing. Johnston and Mohide and Fowler also identified that preceptors must actively teach and support the new nurse in identifying their own learning needs (8, 9).

Entry-level nursing education is grounded in the nursing process (i.e., assess, plan, implement, and evaluate). The education process is very similar, with the focus moved to staff rather than patients. While patient education and patient teaching are often a component of clinical requirements in school, teaching/precepting peers is not routinely addressed, even at the bachelor’s degree level. Therefore, staff nurses need to have preceptor training before they precept. Another finding from our study was recognizing that the role of the preceptor included both leadership and socialization of the new staff nurse. Dusaj and Hilli et al described socialization of the new hire as an important function for the preceptor (3, 4).

Dusaj described developing a tool box of resources for the preceptor (4). Two participants from this study chose to develop a resource manual for their unit during the 2 months between the surveys when they were unable to put their learning into practice. This suggests that they recognized the ongoing process of precepting and the value of having resources to support staff new to the role.

The experienced nurse is often from a different generation than the new staff nurse/student. Therefore, there may be significant differences in the learning styles of the two groups. Preceptors must be able to recognize the strengths and weaknesses of each preceptee to ensure that educational needs are met. This may be quite different from patient teaching because often the patients are of the older generation, possibly similar to the experienced nurse, therefore having complementary learning styles. These generational differences work backwards if the younger nurse is precepting someone from an older generation. Chen’s observation that preceptors should have experience in the clinical area supports the thought that the preceptor and preceptee may be of different generations, with different priorities and values (6). Our study results suggest that the course participants recognized the impact of generational differences in the nursing workforce.
Acknowledgments

The authors thank Chandler Carroll for her assistance with manuscript preparation.


Avocations

It is Never Easy

White coat became a vise.
She was younger than my daughters.
I was replaying the taxing moment.
How to say: “You have leukemia.”

To bar static, I had spun a cocoon
while streetlights whizzed by.
Unsnarled cobwebs woven by her stares
as I rewound the hospital scene.

Reflecting how I walked the tight rope:
I had lumbered to her room,
balancing art against science,
afraid to utter ill-fitting words.

Room was a cave of darkness.
Beams of concern and inquiry
crisscrossed thickness of the air.
I could have clawed under the layers.

Her vagrant eyes combed the desert.
I paused, devising ways to connect:
hands tucked in my pockets,
inessential stethoscope choking my neck.

Chards of dismay in the mouth,
I proceeded to assure: “I have led this trail before—
across the cliffs and canyons
lies the valley of conquerors.”

“I can read your face,” she announced.
“We can fight it.” She drummed out her grief,
offering me a rose of solace
while her finger pads bled.

Copyright © 2016 by Amanullah Khan, MD, PhD. Dr. Khan (e-mail: aman1963@gmail.com) is a member of the Poetry Society of Texas and an oncologist on the medical staff of Baylor Medical Center at McKinney.
Electronic cigarettes (e-cigarettes) are an increasingly popular source of nicotine and an increasingly popular topic in the media. Concerns about potential hazards associated with e-cigarette use and advertising, especially to adolescents, have led to studies on e-cigarettes in both traditional media (TV, mail, print, and outdoor advertising) and social media (websites, social networking sites, blogs, and e-mails). This review presents a narrative description of available studies related to e-cigarettes in the media. These articles have focused on promotion in both traditional and social media across a broad range of topics and have concentrated on target audiences, smoking cessation, harm reduction, and advertising. E-cigarette advertising is the most frequent topic in the published articles. Identifying the target audience also is a common objective in articles. The representation of e-cigarettes as a “healthier alternative” to traditional cigarettes and their use as a “smoking cessation aid” are main themes presented through all types of media.

**METHODS**

A PubMed search was performed for articles published from January 1, 2007, to January 31, 2016, using the following search terms within titles/abstracts: “electronic cigarette*,” “e-cig*,” “electronic nicotine delivery,” “electric nicotine delivery device*,” “ENDD,” “electric cigarette*,” “electric nicotine delivery,” and “electric nicotine delivery device*.” A total of 721 articles were found, and the titles were reviewed to identify potential articles relevant to media, defined as outlets for mass communication. This list was then reviewed for articles related to media. Twenty-seven articles were found, reviewed, and summarized.

**RESULTS**

The 27 relevant articles were reviewed for similarities and trends. Characteristics, such as media type, study type, population, date of study, harm reduction claims, and smoking cessation claims, were extracted and, if relevant, recorded in the Table. These studies analyzed both traditional and social media. Social media were defined as Internet, e-mail, mobile devices, blogging, or social networking sites; traditional media were defined as television, print, radio, direct mail, and outdoor signs. All studies were supported by governmental agencies, universities, or nongovernmental health-related organizations.

Ten of the 27 publications (35%) analyzed traditional media (television, newsprint, product placement, and packaging). Specifically, three articles (11%) studied product placement in retail stores, two articles (7%) focused on newspapers, one article (4%) focused on product packaging, and four articles (15%) considered television advertising. Fifteen publications reported on information from social media, including websites or online presence (seven articles, 26%), Twitter (four articles, 15%), and YouTube (four articles, 15%). Two publications considered all forms of media.

The publications were analyzed for common topics and themes. Most articles (22, 81%) discussed advertising; 8 articles (30%) concentrated on target audience. Other topics included smoking cessation (22%), harm reduction (15%), and prevalence/perception in the media (19%).

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<thead>
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<th>Type of media</th>
<th>Study focus</th>
<th>Study description</th>
<th>Population</th>
<th>Conclusion</th>
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<td><strong>Social media</strong></td>
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<tr>
<td>Online</td>
<td>Advertising, audience (15)</td>
<td>Collection of online banner/video ads</td>
<td>–</td>
<td>30% price promotion; 35% youth as audience</td>
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<tr>
<td>Online</td>
<td>Advertising (28)</td>
<td>Views of online ads</td>
<td>3253 smokers</td>
<td>Interest in e-cig highest when viewing ads about differences from regular cigarettes</td>
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<tr>
<td>Online</td>
<td>Advertising, cessation, harm reduction (26)</td>
<td>Description of ad claims on retail websites</td>
<td>59 sites</td>
<td>88% claimed e-cigs could be smoked anywhere; 95% addressed harm reduction; 64% addressed cessation</td>
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<td>Online</td>
<td>Advertising, cessation, harm reduction, audience (25)</td>
<td>Coding guide analysis</td>
<td>–</td>
<td>89% addressed harm reduction; 67%, cessation; targeted youth/women</td>
</tr>
<tr>
<td>Online</td>
<td>Target audience (17)</td>
<td>Online survey</td>
<td>17,522 adults in 2013</td>
<td>86% aware of products; 47% heard through media channels</td>
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<tr>
<td>Online</td>
<td>Prevalence/perception (30)</td>
<td>Online survey, questionnaire</td>
<td>4618 participants</td>
<td>Variability in flavors was very important to current e-cig smokers</td>
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<td>Online</td>
<td>Advertising, cessation (5)</td>
<td>Survey data</td>
<td>1198 smokers 16 and older</td>
<td>Significant increase in noticing e-cig ads between 2013 and 2014</td>
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<tr>
<td>Twitter</td>
<td>Prevalence/perception in media (16)</td>
<td>Content analysis</td>
<td>7362 tobacco tweets</td>
<td>46% tweets positive</td>
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<td>Twitter</td>
<td>Advertising, prevalence/perception, cessation (18)</td>
<td>Keywords in tweets related to e-cig</td>
<td>73,672 tweets; 90% commercial</td>
<td>Small group of highly active commercial accounts; 10% addressed cessation</td>
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<td>Twitter</td>
<td>Advertising (31)</td>
<td>Twitter data analysis</td>
<td>1.7 million tweets 2008–2013</td>
<td>Most tweets were advertising (93%); e-cig tweets increased 10× from 2009 to 2010</td>
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<tr>
<td>Twitter</td>
<td>Advertising, cessation (17)</td>
<td>Twitter data survey</td>
<td>17,522 adults in 2013</td>
<td>US adults are widely exposed to e-cig marketing through the media</td>
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<tr>
<td>YouTube</td>
<td>Prevalence/perception in media (24)</td>
<td>Video data from YouTube</td>
<td>–</td>
<td>Puff duration longer in e-cig users</td>
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<tr>
<td>YouTube</td>
<td>Prevalence/perception, harm reduction (19)</td>
<td>Top 20 search results</td>
<td>196 videos</td>
<td>94% pro; 2% anti; 71.4% cessation</td>
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<tr>
<td>YouTube</td>
<td>Advertising (23)</td>
<td>Content analysis</td>
<td>365 videos</td>
<td>85% sponsored by market; highlight economic/social benefits</td>
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<td>YouTube</td>
<td>Advertising, target audience (20)</td>
<td>Online survey on videos</td>
<td>2068 adolescents</td>
<td>E-cigs in 2% (95% CI, 0–4%)</td>
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<td><strong>Traditional media</strong></td>
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<td>Television</td>
<td>Advertising, cessation, target audience (14)</td>
<td>Measurement of awareness and receptivity</td>
<td>519 adult smokers</td>
<td>Prior e-cig users more receptive; 74.6% of surveyed thought of cessation</td>
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<tr>
<td>Television</td>
<td>Advertising (12)</td>
<td>Analysis of Nielsen data</td>
<td>Youth</td>
<td>Exposure increased 256%; 76% on cable; ad for 1 brand</td>
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<tr>
<td>Television</td>
<td>Advertising (21)</td>
<td>Online survey</td>
<td>5020 youth</td>
<td>After exposure, youth perceived e-cigs as cooler, fun, healthier, and enjoyable</td>
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<tr>
<td>Television</td>
<td>Advertising (22)</td>
<td>Observational survey</td>
<td>296 students at US university</td>
<td>Students exposed to ads had positive reaction to the ads</td>
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<tr>
<td>Newsprint</td>
<td>Harm reduction (32)</td>
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<td>478 news media articles</td>
<td>Rising presence in media; conflict over harm reduction vs. increased initiation</td>
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<tr>
<td>Newsprint</td>
<td>Prevalence/perception (10)</td>
<td>Thematic analysis</td>
<td>12 papers/3 web news</td>
<td>Increased coverage substantially</td>
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<tr>
<td>Product placement</td>
<td>Advertising (6)</td>
<td>Observational; descriptive study</td>
<td>Assessments in 320 retail stores</td>
<td>Availability more than doubled; presence of ad signs increased</td>
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<td>Product placement</td>
<td>Advertising, target audience (7)</td>
<td>Observational</td>
<td>Audits of 108 stores</td>
<td>Not related to store size; trend toward increased availability in more deprived areas</td>
</tr>
<tr>
<td>Product placement</td>
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<td>Observational; audits of retailers</td>
<td>Study 1, 2165; Study 2, 2526</td>
<td>Availability more likely in areas with weak tax and smoke-free air policies</td>
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<tr>
<td>Packaging</td>
<td>Advertising (11)</td>
<td>Randomized trial; view of print ads</td>
<td>483 nontobacco users</td>
<td>Graphic label depicting “low risk”</td>
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</table>

**All media**

<table>
<thead>
<tr>
<th></th>
<th>Study focus</th>
<th>Study description</th>
<th>Population</th>
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<tr>
<td>All media</td>
<td>Advertising, target audience (27)</td>
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<tr>
<td>All media</td>
<td>Advertising (33)</td>
<td>Observational study</td>
<td>1449 US adults</td>
<td>Discussion associated with lower perceived harm of second-hand vapor</td>
</tr>
</tbody>
</table>
DISCUSSION

The number of articles published on e-cigarette promotion in both traditional and social media has steadily increased since its introduction (5). Ten articles focused on traditional media. During the period from 2012 to 2013, the availability of e-cigarettes in retail stores more than doubled, with most retail stores selling the devices and with advertising closely resembling former tobacco industry market strategy (6–8). E-cigarette companies tend to place this product in stores in higher-income neighborhoods and in locations with smoke-free air regulations (9). Newspaper advertising strategy seems to focus on five similar themes: smoke-free legislation, risk and uncertainty, healthier choice, celebrity use, and price (10). Traditional tobacco products are required to place warning labels on their products. E-cigarette packaging, misleadingly, has placed labels claiming a low risk on their products (11). E-cigarette companies also advertise their products to an increasingly broad television audience, including youth, utilizing primarily national cable networks (12, 13). Commercial frequency increased 256% in the period from 2011 to 2013 (12, 13). With this increase in availability, there is an increase in public appearance and normalization of smoking behavior (7, 14).

Fifteen articles focused on social media and e-cigarettes. Over $2 million is spent a year in e-cigarette advertising via media in the US and Canada alone (15). Twitter, an online social networking service with 302 million active users, is used as a marketing tool for manufacturers of e-cigarettes and other tobacco products with e-cigarette “tweets” increasing 10-fold from 2009 to 2010, 93% being advertising (16). E-cigarette companies have used tweets to promote their products’ use for cessation and to suggest decreased harm (17). These commercial accounts have been used heavily with the potential to reach millions of Twitter users. Tweets refer to cessation and offer discounts with direct links to commercial websites from which customers can purchase e-cigarettes (18).

YouTube, a video-sharing website with 4 billion video views per day, also offers unique insight into e-cigarette commercial opinions and advertising habits. Most videos depict e-cigarettes as a healthier option than traditional cigarettes or as being more socially acceptable or attempt to prompt branding (19, 20). Social acceptance is an important focus for e-cigarette manufacturers. One survey showed that people perceived e-cigarettes as healthier and “cooler” after watching advertisements (21). While no longitudinal studies are available to support the idea that e-cigarettes cause less harm than traditional cigarettes, up to 85% of videos referencing e-cigarettes are posted for promotion of the product, with information often discussing health and smoking cessation (22, 23). One YouTube article did attempt to study differences in smoking patterns in e-cigarette users compared with traditional cigarette smokers. These authors suggest that e-cigarette users inhale longer, possibly to compensate for the poor nicotine delivery system, but the clinical implications of this pattern, if any, are unclear (24). E-cigarette manufacturers use their own websites to promote e-cigarettes as having health benefits, producing no second-hand smoke, and being a viable option for cessation (25). Ninety-five percent of observed manufacturer websites made explicit or implicit health-related claims, with 64% having a smoking cessation–related claim (26).

Marketing differentially targets specific audiences (17). Baumann et al presented a cross-sectional survey study given to hospitalized patients who were asked to recall their exposure to e-cigarette advertising over the past 6 months. This study showed that Caucasians were more aware of advertising efforts than African Americans and that both cohorts were increasingly exposed over time (27). E-cigarette use has historically been lower in African Americans, yet e-cigarette use has increased in both African Americans and Caucasians in the past decade, with Caucasian use remaining higher (27). Other studies have demonstrated that interest in e-cigarettes increases after exposing the target audience to visual images of their use or to advertising comparing e-cigarettes to traditional cigarettes (15, 28). Both never-smokers and current regular cigarette smokers were targeted as well as younger nonsmokers. Youth traditional cigarette smoking susceptibility has been directly linked to exposure through static advertising. Fulmer and associates recently reported that tobacco advertising in newspapers, magazines, and retail stores and screen tobacco images in television and movies increase tobacco use in a dose-dependent manner in US middle and high school students. In addition, the perception of peer use increases the likelihood of tobacco use in the students. E-cigarette companies have increased advertising to this audience through more use of social media (29).

More information on advertising methods and their effects on consumers would provide better understanding of e-cigarettes’ use and opportunities for public health officials to address health and access issues. Public health organizations should provide information to e-cigarette users and the public through these outlets and take a strong stance against their use, especially by school-aged children.

2. Robehm N. E-cigarette sales surpass $1 billion as big tobacco moves in. Forbes, September 17, 2013.
Electronic cigarettes in the media

Tricyclic antidepressant poisoning remains a major cause of morbidity and mortality, particularly in the setting of suicidal attempts. The current standard of care for treatment is the administration of sodium bicarbonate infusion. Adjunctive lipid emulsion therapy and plasmapheresis have received attention recently. We report an 18-year-old patient who was successfully managed with lipid emulsion and plasmapheresis as adjuncts to sodium bicarbonate treatment and review some of the recent literature.

Tricyclic antidepressant (TCA) poisoning presents a tremendous management challenge (1). While the selective serotonin receptor inhibitors are now increasingly prescribed for the treatment of depression, TCAs still play a role in the treatment of other conditions including enuresis, obsessive compulsive disorder, attention deficit hyperactivity, separation anxiety and neuralgic pain in children, and chronic pain and migraine in adults. Patients with suicidal ideation still seek TCAs as a way of attempting suicide (2). If abused, euphoria, hallucination, and a distorted sense of time may result (1). TCA overdose often represents a dire emergency with high mortality rates. The mainstay of management is the administration of intravenous sodium bicarbonate. Recently, adjunctive therapies, including intravenous lipid administration and emergent plasmapheresis (3–7), have been increasingly used. We present a case of amitriptyline overdose with suicidal intent in a young patient with major depression.

CASE PRESENTATION

An 18-year-old man was brought to the emergency department after being found unresponsive at home with empty bottles of amitriptyline and venlafaxine. He had a medical history of severe depression and attention deficit hyperactivity disorder, with three prior suicide attempts. His parents were not sure how many pills he had ingested. In the emergency department, he was minimally responsive to painful stimuli with sonorous respirations. His initial oxygen saturation was 70%. An initial electrocardiogram showed a widened QRS, prominent R waves in aVR, and frequent ventricular premature complexes (Figure 1). Within minutes of arrival, he went into cardiac arrest from ventricular fibrillation. He also had a witnessed generalized tonic clonic seizure during the episode of cardiopulmonary resuscitation. He was successfully resuscitated after receiving five rounds of intravenous epinephrine, shocks, and two rounds each of naloxone and 8.4% sodium bicarbonate. The patient was responsive immediately upon return of spontaneous circulation. He was then treated with activated charcoal to attempt gastric decontamination and 20% intravenous lipid emulsion before being transported to the intensive care unit and continued on a sodium bicarbonate infusion.

Arterial blood gas analysis showed anion gap metabolic acidosis and respiratory acidosis. The patient was also treated with plasmapheresis on two occasions for the next two consecutive days. He remained hemodynamically unstable, requiring ventilator support and vasopressors. We also administered 2 g of intravenous magnesium sulphate to reduce the risk of recurrent ventricular arrhythmias. Serial 12-lead electrocardiograms were used to monitor his QT interval. His urine was positive for opiates and phencyclidine. Laboratory assay for acetaminophen and salicylate were unremarkable. An initial electrolyte panel revealed a serum potassium level of 5.8 mmol/L and serum creatinine of 2.39 mg/dL (reference range, 0.7–1.3), increased from his baseline of 0.93. The creatine kinase was 7350 U/L (reference range, 30–170) on presentation, peaking to 8162 on day 2.

In spite of aggressive treatment, the patient developed clinical and radiologic features of acute respiratory distress syndrome (ARDS). Serial chest x-rays showed extensive bilateral airspace opacities consistent with ARDS. He initially received intravenous vancomycin and piperacillin tazobactam for 7 days, but on account of inadequate clinical response was changed to aztreonam and clindamycin with better clinical response. Our patient improved gradually over the next 15 days. After his acute kidney injury, rhabdomyolysis, and ARDS resolved, he was discharged to the psychiatry unit for further management of his severe depression.

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DISCUSSION

Our patient unsuccessfully attempted suicide with amitriptyline and possibly other medications. It has been estimated that 97% of the deaths from antidepressants are from TCAs (1–3). Our patient manifested classic clinical complications of TCA overdose, specifically the development of life-threatening arrhythmias (QRS prolongation, ventricular tachycardia/fibrillation), seizures, and hypotension. He also developed rhabdomyolysis, acute kidney injury, and ARDS, which although not as common have been reported following TCA overdose. Rhabdomyolysis has been reported as a rare complication following TCA overdose (8). The Table reviews other cases of TCA overdose, describing the patient’s clinical features, as well as the interventions and their outcomes (3, 5, 9–16).

Ventricular fibrillation following TCA overdose has been reported in about 2% to 4% of cases and is more common in severe poisonings involving extreme QRS widening and QT prolongation (1). Our patient had very impressive QRS prolongation, up to 170 ms. QRS duration is thought to be a better predictor of morbidity than the plasma level of the TCA (1, 17). A duration >160 ms predicts a 50% chance of life-threatening ventricular arrhythmias (1, 17). A QRS duration >100 ms is an indication for bicarbonate therapy in the setting of TCA overdose (1). Electrocardiographic signs suggestive of toxicity include QRS duration >100 ms, abnormal QRS morphology, and abnormal size and ratio of the R and S waves in lead AVR, specifically R wave in AVR >3 mm and R to S ratio in AVR >0.7. Other cardiac manifestations of toxicity include the development of a bundle branch block, commonly a right bundle branch block (1, 17).

The TCAs exert their pharmacologic effects by the inhibition of presynaptic serotonin and norepinephrine uptake. TCAs are rapidly absorbed from the gut and reach high plasma levels within 2 to 8 hours. They have a high volume of distribution on account of their high lipid solubility. In plasma, TCAs circulate bound to alpha 1 acid glycoprotein. They undergo phase 1 metabolism in the liver with the action of the CYP2D6 en-
zyme and also glucuronidation (1). In the setting of an overdose, the clinical consequences are thought to be due to the ability of TCAs to block cardiac fast sodium channels and antagonize the central and peripheral muscarinic acetylcholine receptors, peripheral alpha adrenergic receptors, histamine H1 receptors, and central nervous system GABA A receptors. The clinical picture is also compounded by the presence of significant drug enterohepatic circulation and active metabolites of the drug following glucuronidation. It is difficult to predict drug kinetics when dosed therapeutically, as other effects such as acidemia, CYP2DC saturation, and decreased gut motility (from anticholinergic effects) help potentiate drug action (1).

Based on the clinical circumstances, our patient received treatment with activated charcoal for gastric decontamination, intravenous sodium bicarbonate, lipid rescue, and plasmapheresis. He was also intubated and mechanically ventilated initially for airway protection following cardiopulmonary resuscitation and then for management of ARDS. His refractory hypotension was treated with intravenous fluids and vasopressors, fluid administration being adjusted as appropriate because of the concomitant ARDS.

ARDS following TCA overdose has been reported frequently in the literature over the last 20 to 30 years (18, 19). The exact mechanisms at play are not clearly defined but may relate to the effects of prolonged hypotension, aspiration of gastric contents, sepsis, and direct action of the drugs on the lung parenchyma. We treated our patient with antibiotics in the belief that he aspirated during the acute phase of TCA toxicity, as his mental status rapidly deteriorated with concomitant seizures and cardiopulmonary arrest and subsequent cardiopulmonary resuscitation.

Treatment with sodium bicarbonate remains the standard of care for TCA poisoning (1). This induces an alkalosis and provides a sodium load that helps improve cardiac conduction. The sodium loading also helps treat the ensuing hypotension seen in many patients. Alkalosis helps reduce the amount of free drug by increasing protein binding. However, the toxicity profile and the clinical instability of some patients in spite of sodium bicarbonate administration have necessitated the trial of other adjunctive therapies such as lipid emulsion treatment and plasmapheresis, as with our patient. In view of the lack of randomized trials that have demonstrated effectiveness, these treatments remain controversial and are not yet recommended by the standard treatment guidelines (1, 20). Another issue that presents a dilemma to clinicians is the fact that there is no certain method to determine that sodium bicarbonate has failed and that other treatments need be instituted. Clinicians tend to initiate other treatments depending on disease severity.
Table. Published cases of tricyclic antidepressant overdose

<table>
<thead>
<tr>
<th>Report and country</th>
<th>Patient demographics and presenting complaint</th>
<th>Patient key clinical features</th>
<th>Initial interventions</th>
<th>Definitive interventions and clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hendron, 2011, N. Ireland (9)</td>
<td>20-mo F, 45 mg/kg dosulepin</td>
<td>Drowsy, nystagmus, BP 80/40, HR 130, seizures</td>
<td>Diazepam, thiopentone, gastric lavage, sodium bicarbonate</td>
<td>ILE at 1 mL/kg then infusion of 150 mL/h for 1 h; discharged on day 3</td>
</tr>
<tr>
<td>Boegevig, 2011, Denmark (10)</td>
<td>36-γ F, 5.25 g dosulepin</td>
<td>GCS 12, tachycardia, QRS 120 ms, seizures</td>
<td>Diazepam, propofol, sodium bicarbonate</td>
<td>ILE at 1.5 mL/kg (100 mL), then 400 mL over 20 min; QRS shortened, discharged on day 3</td>
</tr>
<tr>
<td>Nair, 2013, UK (11)</td>
<td>34-γ F, 5.6 g amitriptyline and 2.4 g citalopram</td>
<td>GCS 3, BP 51/29, seizures, QRS 171 ms, VT</td>
<td>Diazepam, epinephrine, sodium bicarbonate</td>
<td>20% ILE at 1.5 mL/kg, then infusion for 60 min; complete recovery within 24 h</td>
</tr>
<tr>
<td>Karaci, 2013, Turkey (5)</td>
<td>15-γ F, 22 mg/kg amitriptyline</td>
<td>GCS 5, depressed respi- rations and reflexes</td>
<td>Intubation, gastric lavage, sodium bicarbonate</td>
<td>Plasmapheresis for 4 h; GCS improved to 13</td>
</tr>
<tr>
<td>Blaber, 2012, UK (12)</td>
<td>36-γ F, 2.25 g of dothiepin</td>
<td>GCS 4, BP 53/35, HR 130, pH 6.75, QTC 502</td>
<td>IV fluids, gastric lavage, sodium bicarbonate, amioda- rone, transvenous pacing</td>
<td>1.5 mL/kg/min of 20% ILE then 400 mL infusion; sinus rhythm and complete recovery</td>
</tr>
<tr>
<td>Agarwala, 2014, USA (13)</td>
<td>44-γ M, 2.25 g of amitriptyline</td>
<td>Unconscious, BP 65/42, QRS 160, seizures, PEA</td>
<td>Warming, vasopressors, sodium bicarbonate</td>
<td>20% ILE as 250 mL bolus followed by infusion; QRS duration decreased, BP stabilized</td>
</tr>
<tr>
<td>Scholten, 2012, Netherlands (14)</td>
<td>53-γ F, amitriptyline, citalopram, and venlafaxine</td>
<td>GCS 3, RR 8, BP 75/35, idioventricular rhythm</td>
<td>Intubation, activated charcoal, sodium bicarbonate</td>
<td>20% lipid emulsion; narrowing of QRS complex and sinus rhythm, patient recovered</td>
</tr>
<tr>
<td>Harvey, 2012, New Zealand (5)</td>
<td>51-γ M, 43 mg/kg amitriptyline, possibly quetiapine, citalopram, metoprolol, quinapril, aspirin</td>
<td>GCS 3, HR 150, BP 112/82, QRS 180 ms, wide complex tachycardia</td>
<td>Sodium bicarbonate, intuba- tion, gastric lavage</td>
<td>100 mL 20% lipid emulsion, then 400 mL over 30 min; QRS narrowed, HR and BP stabilized</td>
</tr>
<tr>
<td>Levine, 2012, USA (15)</td>
<td>13-γ F, unknown quantities of amitriptyline</td>
<td>RR 6, QRS 176 ms, QTC 477, seizure, cardiac arrest</td>
<td>Intubation, sodium bicarbon- ate, lorazepam, midazolam, epinephrine, phenobarbital</td>
<td>1.5 mg/kg of 20% ILE, continuous infusion of 0.25 mg/kg/min for 30 min; patient survived</td>
</tr>
<tr>
<td>Koschmy, 2014, Germany (16)</td>
<td>21-γ F, carvedilol, amiodrine, amitriptyline, torsemide, ketoprofen, nicotinic acid, gabapentin</td>
<td>Asystole, CPR with ROSC</td>
<td>ECMO, temporary pacing, plasmapheresis</td>
<td>Weaned from ECMO on day 4, extubated on day 8; no neurological sequelae</td>
</tr>
</tbody>
</table>

BP indicates blood pressure (mm Hg); CPR, cardiopulmonary resuscitation; ECMO, extracorporeal membrane oxygenation; F, female; GCS, Glasgow coma score; HR, heart rate (beats/ min); ILE, intralipid emulsion; M, male; PEA, pulseless electrical activity; ROSC, return of spontaneous circulation; RR, respiratory rate (breaths/min); VT, ventricular tachycardia.

and response of electrocardiographic and hemodynamic parameters (1).

Lipid emulsion therapy is thought to work by countering the activity of lipophilic drugs, like the TCA drugs. Its use was first demonstrated in anesthetic agent overdose and gradually began to be used in TCA poisoning. It is thought to be able to sequester the ingested TCAs. There are multiple case reports of dramatic clinical response in cases of severe TCA poisoning managed with adjunctive intralipid administration in addition to sodium bicarbonate infusion (3, 7, 20).

Plasmapheresis involves the removal of the patient’s plasma and replacement with another fluid (e.g., allogeneic donor plasma, colloid, crystalloid). This is useful in TCA poisoning because of the high lipid solubility and binding of TCAs. Reductions in plasma levels as much as 63% have been reported after plasmapheresis for TCA poisoning (5). The use of plasmapheresis in TCA poisoning has been controversial; while several case reports have suggested good outcomes following its use (1, 5, 6, 16), the Extracorporeal Treatments in Poisoning (EXTRIP) Working Group recommended against the use of plasmapheresis and extracorporeal treatment for TCA poisoning, citing the insufficient data regarding the benefits and effectiveness of plasmapheresis (8). Our report adds to the collection of clinical case reports where adjunctive plasmapheresis and lipid rescue have been associated with a good outcome in TCA overdose.

Acknowledgments

We thank Dr. Theophilus Ekpong Owan of the Division of Cardiology, Department of Medicine, University of Utah School of Medicine, Salt Lake City, for his help with revising the draft of our manuscript.

We present a case of hypersensitivity pneumonitis caused by intranasal abuse of the prescription narcotic hydrocodone. The patient’s clinical course was complicated by acute respiratory failure. A chest radiograph showed diffuse bilateral opacities. The patient was treated with noninvasive ventilation, a high dose of intravenous steroids, and bronchodilators, resulting in improvement of symptoms and radiographic appearance.

A common controlled prescription drug for pain is oral hydrocodone. According to a report from the National Center on Addiction and Substance Abuse at Columbia University, 99% of all hydrocodone in the world is used in the USA (1). Snorting is a new route of hydrocodone abuse, which results in a rapid onset of effects, causing almost immediate pain relief and euphoria. But when the drug is snorted, there is a much greater risk of toxic effects, including hypersensitivity pneumonitis causing respiratory failure. Such was the case in the patient described herein.

CASE DESCRIPTION

A 52-year-old Native American woman came in with symptoms of dyspnea, wheezing, hypoxia, dry cough, and subjective fever. She was a chronic smoker. She previously had coronary artery bypass graft and stenting at an outside facility. She reported snorting hydrocodone daily for the last 2 months.

On examination she was afebrile, tachypneic, and hypoxic on room air, with an oxygen saturation of 84%. Chest exam revealed wheezes. She had mild leukocytosis and a normal metabolic panel, cardiac panel, D-dimer, and brain natriuretic peptide (Table 1). A chest radiograph showed diffuse patchy areas of ground-glass airspace disease bilaterally (Figure 1).

High-resolution lung computed tomography showed mosaic attenuation of lungs with scattered areas of ground-glass opacity interspersed with more lucent areas of lung along with mild paraseptal emphysema (Figure 2). An echocardiogram showed normal left ventricular function with no regional wall motion abnormality.

The patient was treated with high-flow oxygen, bronchodilators, and high-dose intravenous steroids. She was also started empirically on antibiotics. The following day she remained dyspneic and hypoxic with an increased oxygen requirement of 8 L/min. She was started on noninvasive ventilation for acute respiratory failure.

Her dose of methylprednisolone was increased to 125 mg every 6 hours. Her condition gradually improved, and she was weaned off the bilevel positive airway pressure machine. She was

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
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</thead>
<tbody>
<tr>
<td>Leukocyte count (×10⁹/L)</td>
<td>11.5</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dL)</td>
<td>8</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.8</td>
</tr>
<tr>
<td>Brain natriuretic peptide (pg/mL)</td>
<td>50</td>
</tr>
<tr>
<td>Troponin (ng/mL)</td>
<td>&lt;0.012</td>
</tr>
<tr>
<td>D-Dimer (mg/L)</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Table 1. The patient’s laboratory values

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discharged from the hospital with near complete resolution of her symptoms. She was switched to oral prednisone, which was tapered during the next 2 weeks. A follow-up chest radiograph showed complete resolution of the infiltrate.

**DISCUSSION**

Hypersensitivity pneumonitis, also called extrinsic allergic alveolitis, is an immunologic reaction to a wide variety of inhaled organic and inorganic antigens. These include but are not limited to microorganisms (bacteria, fungi, mycobacteria, and virus), agricultural aerosols, animal protein, and many chemical reagents. Recurrent exposure leads to chronic inflammation and fibrotic lung disease. Therefore, early diagnosis and avoidance of the exposed allergen is the key to treatment.

Patients are exposed to these allergens as a result of their occupation or lifestyle. Dyspnea, dry cough, fever, weight loss, and easy fatigability are the most common presenting symptoms (2). Acute symptoms are seen within 4 to 12 hours of antigen exposure and are alleviated by removal of the offending agent. Repeat exposure after abstinence often causes recurrence of the symptoms. The disease presentation, severity, and latency are influenced by the concentration of the inhaled antigen, duration of exposure, frequency of exposure, and interval between exposures.

Several different criteria for diagnosis of hypersensitivity pneumonitis have been described, but they were developed before the advent of high-resolution computed tomography and bronchoalveolar lavage. They are usually for acute cases and depend on an abnormal chest radiograph or positive serum precipitins, which are often absent (3–5). Most of the diagnostic criteria include one or all of the following: (1) known exposure to the antigen; (2) compatible clinical, radiographic, and physiologic findings; (3) positive inhalation challenge test; (4) histopathology changes of noncaseating granuloma or mononuclear infiltrate or bronchoalveolar lavage with lymphocytosis. Imaging studies including chest radiograph and high-resolution computed tomography show reticulonodular and/or ground-glass opacities. Chronic cases due to repeated exposure show fibrotic changes with volume loss (6).

In our patient, the antigen was inorganic powdered hydrocodone, which after snorting triggered a severe allergic response leading to hypersensitivity pneumonitis and acute respiratory failure. Continued recreational abuse by patients over time could lead to parenchymal lung fibrosis. Drug counseling and rehabilitation should be part of overall management.

Pyomyositis is an acute infectious disorder affecting the skeletal muscle. Although seen more commonly in the tropics, cases are being reported in temperate countries, including the United States. We report a case of nontropical pyomyositis in a 58-year-old diabetic man who presented with a vague chest wall swelling. His initial clinical presentation and imaging findings suggested an intramuscular hematoma. He later developed fever with increased swelling, and pyomyositis was diagnosed after aspiration of the swelling yielded *Streptococcus agalactiae*. Aspiration of the abscess and the use of appropriate antibiotics led to complete resolution of the disease. We discuss possible factors in diabetics that might predispose them to pyomyositis.

Pyomyositis is a primary supplicative infection of the skeletal muscle occurring in the absence of adjacent bone, soft tissue, and skin involvement. This entity was first described as an endemic disease of the tropics by Scriba in 1885 (1). Since then, many reports have emerged in temperate climates, with the first case in the US described in 1971 (2). We present the case of a 58-year-old man with a history of Hodgkin's lymphoma and diabetes who developed an acute swelling of the chest wall that was ultimately diagnosed as pyomyositis.

**CASE REPORT**

A 58-year-old man presented with a painful swelling of the right chest wall of 1 week duration. He denied fever, chills, night sweats, or recent trauma to that area and had no cough or dyspnea. His pain radiated from his chest to the right axilla and shoulder and increased with active movement of his arm. At the age of 51, the patient was diagnosed with Hodgkin's lymphoma, with extensive lymphadenopathy in the right inguinal area extending to the right iliac vein. He completed chemotherapy and radiation therapy to the right inguinal and pelvic areas and had been in remission for the past 5 years. A computed tomography (CT) scan of the chest, abdomen, and pelvis done 1 week prior to admission as part of surveillance was normal. His vital signs were within normal limits. He had a poorly defined 8 × 8 cm tender erythematous mass involving his right chest wall with a soft consistency. The mass centered around an old surgical scar from a port-a-cath that was removed a year earlier. There were no enlarged lymph nodes. Lungs were clear to auscultation, and the rest of the physical examination was within normal limits. The white blood cell count was 16.8 × 10^9/L with a left shift and 82% neutrophils. A random blood sugar was 310 mg/dL, and the hemoglobin A1c level was 10.4%. Blood cultures were negative. An ultrasound revealed a diffuse soft tissue swelling with no evidence of an abscess. A CT of the chest with contrast demonstrated a nonspecific fluid loculation measuring 5.0 × 2.8 cm between the right pectoralis major and minor muscle (Figure). On day 3, the patient spiked a temperature of 100.5°F with an increase in the size of the swelling. An ultrasound-guided incision and drainage was done, and 35 mL of thick pus was aspirated. The culture from the aspirate grew *Streptococcus agalactiae*. He was treated with 4 weeks of intravenous antibiotics resulting in good clinical improvement. There was no recurrence of symptoms on follow-up a month later.

**DISCUSSION**

Pyomyositis is an acute bacterial infection reported in young healthy children and adults residing in the tropics. The
nontropical entity seen in temperate climates is more common in older patients and in those with immunocompromising diseases, such as HIV, diabetes mellitus, malignancies, autoimmune disorders, and chronic liver disease (3, 4). The pathogenesis of pyomyositis is poorly understood. Prior muscle injury and transient bacteremia probably contribute to its development (5). The fibronectin-binding receptors on muscle cells are possible pathways for bacterial entry (6). Muscles frequently involved are the large muscle groups, like the quadriceps, glutei, and trunk muscles (7). *Staphylococcus aureus* is the most common organism isolated (5, 7). The other rare causative organisms include *Streptococcus* groups B and C, gram-negative organisms including *Escherichia coli* and *Klebsiella* species, anaerobic bacteria, *Mycobacterium* species (*M. avium* complex and *M. tuberculosis*), and fungi (5, 6, 8). Pyomyositis is often misdiagnosed in its initial stages, as the clinical presentation is similar to muscle hematoma, cellulitis, osteomyelitis, and thrombophlebitis. The diagnosis is facilitated by radiologic techniques that can demonstrate the presence of fluid collections, and contrast magnetic resonance imaging is the preferred technique (9). Definitive treatment includes drainage of the abscess and long-term intravenous antibiotic therapy.

This patient developed pyomyositis at the site where he had a prior port placed for chemotherapy, which might represent an area of local muscle injury. His diabetes was uncontrolled with a hemoglobin A1c of 10.9%. In a review of 246 cases of pyomyositis in non–HIV infected patients, diabetes mellitus was the most common association seen (6). Diabetes mellitus may predispose a patient to muscle damage and various bacterial infections. Microangiopathic changes and large vessel atherosclerosis are associated with microinfarcts in the muscle (10). The subsequent decrease in blood supply and local hypoxia may increase the risk of infection and abscess formation. Markedly thickened basement membranes in capillaries have been noted in diabetics and may inhibit migration of neutrophils (11). Diabetic patients have defective neutrophilic function and defective T cell–mediated immune responses, which make them prone to infections (12–14).

This patient had pyomyositis secondary to *Streptococcus agalactiae*, which was isolated from his aspirate. *S. agalactiae* is known to cause infection in neonates and pregnant women, but rarely causes infection in adults. A PubMed search revealed only 2 cases of pyomyositis in diabetics caused by *S. agalactiae* (15, 16). The patient improved dramatically on 4 weeks of intravenous antibiotic therapy. Prolonged intravenous antibiotic therapy is recommended to avoid mortality and complications such as sepsis and toxic shock syndrome.

Inferior vena cava filter removal after prolonged dwell time of 2310 days

Ankit H. Shah, MD, Andrew Lichliter, MD, and Marco Cura, MD

Inferior vena cava filters are commonly placed for a variety of indications, often when anticoagulation is contraindicated. Although technical success is high and complication rates low, there are complications that are important to be aware of. We present the case of a 29-year-old woman with a prolonged filter dwell time resulting in complications.

Inferior vena cava (IVC) filter placement is designed to prevent pulmonary embolus by trapping venous emboli and has become a relatively common procedure with excellent technical success (99%) (1). Indications for placement are divided into accepted, relative, and prophylactic categories. Accepted indications include documentation of venous thromboembolism (VTE) plus one or more of the following: contraindication to anticoagulation, progression/recurrence of VTE while anticoagulated, complication of anticoagulation, life-threatening pulmonary embolus, and inability to achieve/maintain therapeutic anticoagulation. Optional filters now exist in which a filter can be retrieved percutaneously. Ongoing monitoring and follow-up evaluation to assess anticoagulation status and need for filter are required, as long-term complications exist. Complications include IVC perforation (0%–41%), filter migration (0%–18%), filter fracture (2%–10%), and IVC occlusion (2%–30%) (2). Caval perforation can result in injury to adjacent structures, although most are asymptomatic. Extreme examples include gastrointestinal hemorrhage and aortic dissection (3, 4). Migration of fracture fragments can cause serious complications, such as life-threatening arrhythmias and myocardial perforation with cardiac tamponade (3). The Food and Drug Administration recommends that physicians responsible for the ongoing care of patients with retrievable filters consider removing the filter as soon as protection from pulmonary embolus is no longer needed (5). Filter removal is not always straightforward.

CASE REPORT

A 29-year-old black woman presented with fulminant hepatic failure secondary to autoimmune hepatitis. She developed hyperammonemia with encephalopathy, increased intracranial pressure, and cerebral edema. Cadaveric liver transplantation was performed. On postoperative day 1, head computed tomography (CT) for cerebral edema monitoring revealed right frontal lobe parenchymal hemorrhage. On postoperative day 5, follow-up head CT revealed interval multifocal cortical infarctions. Lower-extremity paresis developed, resulting in prolonged bedrest. Surveillance lower-extremity venous duplex 2 weeks postoperatively was negative.

The patient’s clinicians elected to have an IVC filter placed for prophylaxis in the setting of intracerebral hemorrhage and increased risk of thromboembolic disease secondary to prolonged immobility. A retrievable G2 IVC filter (Bard Peripheral Vascular, Tempe, AZ) was placed via the right common femoral vein percutaneous approach. During the procedure, a venogram identified nonocclusive infrarenal mural thrombus. The filter was placed superior to the thrombus with the filter tip at the renal vein level. This represents the conversion of a prophylactic to an accepted indication, with confirmation of IVC thrombus in the setting of hemorrhage. At implantation, the filter long axis was parallel with the caval wall without tilt. The patient was discharged to a rehabilitation facility. She continued follow-up with the transplant clinic with routine sonographic and Doppler evaluation of the transplanted liver.

Over 6 years later, CT of the abdomen and pelvis performed for an unrelated indication incidentally revealed fracture of two filter struts (Figure 1a). One was located in the retroperitoneum posterior to the abdominal aorta without evidence of aortic perforation (Figure 1b). The second migrated distally and was lodged within a first-order branch of the middle hepatic vein (Figure 1c). The filter was tilted >15° right anterolaterally; however, the tip was not embedded within the caval wall. Multiple struts had caused caval perforation posterolaterally, with tips located within retroperitoneal fat. Interventional radiology was consulted for removal. The length of dwell time was 2310 days. Prior to removal, bilateral lower-extremity venous duplex revealed no evidence of deep venous thrombosis. Indications for filter continuation were no longer present (the patient was now ambulatory, there was no documented deep venous thrombosis, from the Department of Radiology, Baylor Scott & White Health, Dallas, Texas (Shah, Lichliter, Cura) and the Department of Interventional Radiology, Texas A&M Health Science Center (Cura).

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and there was remote hemorrhage). Given preretrieval findings, informed consent was obtained for anticipated complicated retrieval.

In the interventional suite, a vascular sheath was positioned in the right internal jugular vein after ultrasound-guided Seldinger technique access. An IVC venogram confirmed IVC perforation (Figure 2). Conventional snare techniques were unsuccessful at retrieval. An advanced snare technique was then employed. Two coaxial sheaths were positioned over an Amplatz wire (Cook Medical Inc., Bloomington, IN). Two wires were advanced, one anterior and the other posterior to the filter. The anterior wire was exchanged for a snare system. The distal end of the posterior wire was then snared and retracted, capturing the filter (Figure 3a). The filter tip was retracted into the inner sheath. The filter was collapsed within the outer sheath while the tip was stabilized within the inner sheath and then removed. Intraoperative XperCT (Philips Healthcare, Best, Netherlands) confirmed fractured fragments in the retroperitoneum and liver. A postretrieval IVC venogram showed no extravasation of contrast, stable position of the migrated struts (Figure 3b), and mild luminal narrowing at the site of filter implantation. Angioplasty with an 18 mm balloon at the site of luminal narrowing improved luminal diameter and flow on repeat venography. Also on postretrieval venography, stenosis was identified at the superior IVC anastomosis from the transplant surgery, resulting in reflux into the hepatic veins. This stenosis and secondary reflux was the postulated etiology of strut fracture migration to the middle hepatic vein, preventing possible cardiac embolization. All catheters and wires were removed without complication. Hemostasis was achieved by manual compression. The patient tolerated the procedure well and left the interventional suite in stable condition. Prophylactic anticoagulation was initiated.

**DISCUSSION**

This case demonstrates advanced IVC filter retrieval. Advanced retrieval, generally considered to be safe, is characterized by prolonged fluoroscopy time, use of nonstandard retrieval techniques and devices, filter fracture, filter tip embedding in the IVC wall, and retrieval failure (6). Nonstandard techniques include advanced snare maneuvers, laser-assisted sheath tissue ablation, microdissection with rigid or flexible forceps, and combinations of these methods.

How is it that a filter in good position initially can go on to require complicated retrieval? Electron microscopic analysis of filter fracture has identified foreshortening and flattening in vivo motions transmitted from the IVC to the filter (7). Transmitted motion can ultimately result in one of two fracture modes: high-cycle metal fatigue secondary to accumulated damage and metal overload sustained from acute stress (7). Histologic analysis of filter-adherent tissue on removed filters showed neointimal hyperplasia or fibrosis in 96% of cases (7). Once a filter tip or strut abuts the caval wall, neointimal hyperplasia or fibrosis can cause embedding, thus altering the physiologic stress on the filter. To reduce this risk, if there is malposition of a retrievable filter at the time of insertion (e.g., increased tilt), the filter should be removed and a new device inserted (1).
Multiple statistically significant characteristics on pre-retrieval CT imaging can help prospectively identify potential complicated retrievals. These include tilt angle in mediolateral and anteroposterior directions (>15° cutoff), tip embedding (tightly opposed to IVC wall), strut perforation, and dwell time (6). Some characteristics are anecdotally related, such as increased tilt angle and tip embedding. The degree of filter strut perforation is based on a grading system: grade 0, all struts confined within the lumen; grade 1, strut external but immediately adjacent to the IVC wall; grade 2, struts completely outside IVC lumen; and grade 3, struts adjacent to or inserting into an adjacent organ or retroperitoneal structure (6). Identification of these factors can aid in procedure planning, proper consent, and referral to a tertiary center if needed.

Although retrieval success remains high after more than 1 year after implantation (100% in one study), a prolonged dwell time >180 days has a significant increased risk of complicated retrieval (odds ratio, 2.3) (6, 8). Thus, some authors suggest considering preprocedural CT in the setting of prolonged dwell time (6). In the past, our interventional radiology department relied on referrals for removal. Unfortunately, this patient was lost to follow-up without referral as soon as embolic protection was no longer required. In light of growing data regarding long-term complications and success of filter tracking with dedicated clinics, a new system was implemented. With a patient database and tracking by the interventional radiology department, ordering clinicians are contacted after implantation regarding the evaluation of ongoing filter need with encouraged removal. Abdominal radiographs are initiated at 6 months postimplantation to assess for complications. Retrieval rates have continued to increase since initiation of this proactive and structured follow-up. Our case exemplifies prolonged dwell time, grade 3 strut perforation, and increased tilt angle. Prior knowledge of these characteristics on preprocedural imaging allowed for planning of a successful complicated retrieval with advanced snare techniques.

Isolated left posterior insular infarction and convergent roles in verbal fluency, language, memory, and executive function

Parunyou Julayanont, MD, Doungporn Ruthirago, MD, and John C. DeToledo, MD

The posterior insular cortex—a complex structure interconnecting various brain regions for different functions—is a rare location for ischemic stroke. We report a patient with isolated left posterior insular infarction who presented with multiple cognitive impairment, including impairment in semantic and phonemic verbal fluency.

The insular cortex is a hidden structure located in the Sylvian fissure surrounded by the temporal, frontal, and parietal lobes. It is a complex structure interconnecting various brain regions that contribute to autonomic, gustatory, auditory, and speech and language function as well as somatosensory perception and emotional response (1). The arteries supplying the insular area mainly originate from the M2 segment of the middle cerebral artery (2). This article presents a case of isolated left posterior insular infarction (PII) resulting in impairment in multiple cognitive domains.

CASE REPORT

An 80-year-old right-handed man with 13 years of education woke up with a speech problem. Previously, he had childhood poliomyelitis, diabetes mellitus, coronary artery disease, and hypertension. After waking up, he could not speak fluently, although his comprehension was fully preserved. He also had mild right facial drooping and right-sided weakness.

His vital signs and general exam were normal. The body mass index was 25.4 kg/m². He had right facial weakness, word-finding difficulty, and mild dysarthria. Apart from the lower-extremity weakness from childhood poliomyelitis, he had no other motor or sensory deficits.

Magnetic resonance imaging of the head demonstrated an acute infarction in the left posterior insular cortex (Figure 1), and imaging of the neck showed approximately 50% narrowing of the proximal right internal carotid artery. Transthoracic echocardiogram and telemetry were unremarkable. Aspirin 325 mg/day and atorvastatin 40 mg/day were started.

Two days later, the patient’s right facial drooping, dysarthria, and word-finding difficulty completely resolved. He scored 20 out of 30 in the Montreal Cognitive Assessment (Figure 2) (3, 4). A retrieval memory deficit was detected with delayed recall of 0/5 and a Memory Index Score of 8/15 (5). He also had impairment in semantic fluency (7 words in 1 minute) and phonemic fluency (4 words in 1 minute). Impairment in repetition of complex sentences was detected. He did not demonstrate any naming problem when evaluated by the shortened Boston Naming Test (6). Based on clinical interview and the Geriatric Depression Scale (7), he did not have any affective disturbance that could impair his cognition. The Modified Rankin Scale score was 1 at discharge.

Figure 1. Acute left posterior insular infarction demonstrated by (a) apparent diffusion coefficient imaging and (b) diffusion-weighted imaging.
DISCUSSION

Isolated PII is a rare condition. In one study, among 4800 patients with their first episode of ischemic stroke, only 4 patients (0.08%) had isolated insular infarction (8). The findings of multidomain cognitive impairment in this patient suggest that the posterior insular cortex is a convergent structure; thus, the deficits caused by PII are more likely to be the consequence of diaschisis rather than damage of a specialized or isolated center itself (Figure 3).

Due to the complexity of the cognitive process, it is challenging to draw conclusions about the role of the insular cortex in speech production. In one study, the anterior insular cortex was a common area of infarction in all 25 stroke cases with disorder of motor planning in articulation (9). Left PII was previously reported to cause both dysarthria and aphasia in a single case (8). The insular cortex is activated in the phonological process during reading in functional magnetic resonance imaging (10). Executive function is also required in planning of articulation. Therefore, PII may cause a disconnection between the primary and supplementary motor cortex, leading to executive dysfunction of motor speech (8, 11).

The insular cortex is associated with gustatory, visual, and verbal memory (12–14). Patients with a left insular stroke have more impairment in verbal memory and logical memory than patients with a right insular stroke (13). The disruption of the connection between the left temporal lobe and the left insular cortex may play a role in this deficit. Positron emission tomography in healthy volunteers showed a correlation between cerebral blood flow in the insular cortex and the verbal memory task (15). Improvement with cue may imply that the memory impairment was primarily from deficits in retrieval of the previously registered information, not the encoding process.

Phonemic fluency is primarily mediated by the frontal lobe, while semantic fluency requires lexico-semantic memory, which is functioned mainly by the temporal cortex. In 48 patients with a left-hemisphere stroke, voxel-based lesion symptom mapping showed the association between the phonemic fluency task and the insular cortex lesion (16). The left anterior insular infarction was reported to cause executive dysfunction, including impairment of semantic and phonemic fluency, which may be a result of neuronal network disruption between the anterior insula and frontal lobe and/or cingulate regions (17). To the best of our knowledge, this is the first report of a verbal fluency deficit in a patient with an isolated left PII. Since the posterior insular cortex is adjacent to the semantic storage areas, this infarction may cause network disconnection between these areas, resulting in difficulty retrieving previously learned knowledge.

Even though various types of aphasia were reported in strokes involving the insular cortex (8, 18, 19), pure insular infarction with aphasia is very uncommon. Anatomically, the insular lobe is in the central part of the structures that are important in language functions, including the frontal operculum and Wernicke’s area. The disconnection of these structures and insular area may contribute to language dysfunction after insular damage.
The prognosis of the isolated insular infarction is favorable. In a case series, more than half of patients with isolated insular infarction or had minimal deficits within 48 hours, and all had a Modified Rankin Scale score of 0 to 2 at 6 months (18).

Figure 3. The role of the posterior insular cortex and its connecting areas in multiple cognitive domains including phonemic and semantic verbal fluency, speech executive function, language function, and verbal memory. The posterior insular cortex is a convergent structure connecting with multiple brain regions; thus, the deficits caused by posterior insular infarction are more likely to be the consequence of diaschisis than damage to a specialized or isolated center.

Multiple bee stings resulting in ST elevation myocardial infarction (the Kounis syndrome)

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Kounis syndrome consists of angina pectoris or myocardial infarction that is triggered by the release of inflammatory mediators in the setting of an allergic reaction. We present the case of a 61-year-old man who presented to the emergency department with anaphylaxis after being stung by >100 bees. During resuscitation, he subsequently developed ST elevation myocardial infarction.

Acute coronary syndrome is a common disease process seen in the emergency department. Many physiologic stressors can precipitate its acute presentation. Kounis syndrome, also referred to as “allergic angina,” is a rare but increasingly reported cause of acute coronary syndrome. It can be induced by any anaphylactic reaction and thus must be on a differential diagnosis for anyone with chest pain or symptoms of acute coronary syndrome who presents with the surrounding setting of an anaphylactic reaction. This syndrome requires a high degree of clinical suspicion and can be easily overlooked given the dramatic presentation of anaphylaxis.

CASE REPORT

A 61-year-old white man with no documented coronary artery disease but known congestive heart failure (cause uncertain), type II diabetes, tobacco abuse, hypertension, and hyperlipidemia presented to the emergency department via ambulance after having multiple bee stings while riding on his tractor. The patient received diphenhydramine en route for reported dyspnea and arrived in the exam room with diaphoresis, dyspnea, and innumerable bee stings located mainly on his head, face, and arms. He also presented with a large urticarial rash on his back, with >100 bee stingers remaining in his skin (Figure 1). The patient was given 0.3 mg of 1:1000 intramuscular epinephrine in addition to 125 mg intravenous methylprednisolone for anaphylaxis and showed initial improvement.

Two hours after initial evaluation, he began clutching his chest and reported sudden onset of new 10/10 stabbing left-sided chest pain. The initial electrocardiogram (Figure 2a) revealed sinus tachycardia with a right bundle branch block and frequent ventricular premature complexes and fusion beats, as well as intermittent ventricular bigeminy. Repeat electrocardiogram in the setting of chest pain (Figure 2b) disclosed ST elevation in leads II, III, aVF, and V4 to V6. The cardiac catheterization revealed thrombus in the distal right coronary artery, mid left anterior descending artery, and first diagonal of the distal left anterior descending artery. Immediate percutaneous coronary intervention was performed with successful thrombectomy and placement of bare metal stents in the distal right coronary artery and mid left anterior descending artery.

The patient was transferred to the cardiac intensive care unit, where an echocardiogram revealed severe global left ventricular hypokinesis with an ejection fraction of 25%. Dual antiplatelet therapy, optimal medical therapy, and a life vest were provided.

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The patient was later discharged, only to return within a week with severe chest pain after medication noncompliance. He had an ST elevation myocardial infarction, developed ventricular tachycardia, and went into cardiac arrest. The patient was resuscitated and taken back to the catheterization lab, where his left anterior descending artery stents were found to be thrombosed, likely due to noncompliance with antiplatelet therapy. The thrombus was aspirated from the stents and balloon angioplasty was performed. He required ionotropic support. A repeat echocardiogram disclosed that his ejection fraction had dropped to 15% and a left ventricular thrombus was present. His heart failure regimen was optimized and he was started on anticoagulation.

Over the next 5 months, the patient continued to have multiple admissions for decompensated heart failure and a growing list of comorbidities, including health care–acquired infections. His cardiac function continued to decline, with an ejection fraction of 10%.
fraction decreasing to 10%. His symptoms ultimately became refractory to treatment, and he was transitioned to hospice care.

DISCUSSION

The order *Hymenoptera* consists of families of stinging insects, specifically honeybees and bumblebees in the *Apidae* family and wasps and yellow jackets in the *Vespidae* family. In the United States, *Hymenoptera* envenomations are estimated to cause >40 deaths per year (1). The venom of insects within these families consists of histamine and phospholipase A2, which can induce hypersensitive reactions leading to mast cell activation and degranulation. The combined physiologic effects of these envenomations can subsequently result in coronary vasospasm or potentially acute myocardial infarction (2).

The mechanism is a complicated and multifactorial cascade of endogenous allergic mediators. In the anaphylactic degranulation of mast cells, several collagen-degrading and vasoconstricting substances, such as histamines, neutral proteases, arachidonic acid products, platelet-activating factors, cytokines, and chemokines, are locally released. The physiologic result of the above milieu results in the constellation of coronary vasoconstriction, hypercoagulability, and even atheromatous plaque erosion or rupture (3).

There are three commonly described variants of “allergic angina” based on the patient’s current coronary artery status. The type I variant consists of patients without coronary lesions in whom the allergic insult leads to coronary vasospasm with either normal or subsequently elevated cardiac enzymes. The type II variant describes patients with existing athermanous disease. In these patients, an anaphylactic insult leads not only to vasospasm, but to atheromatous plaque rupture and subsequent myocardial infarction. Type III involves coronary artery stent thrombosis, which stains positive for eosinophils and mast cells (4, 5). In the case described above, we suspect an incidence of the type II Kounis syndrome variant, given the patient’s clinical presentation and comorbidities of congestive heart failure, severely uncontrolled diabetes, tobacco abuse, hypertension, and hyperlipidemia.

Rupture of the ventricular septum during acute myocardial infarction usually occurs within the first week. The event is usually followed by low cardiac output, heart failure, and multiorgan failure. Despite the many advances in the nonoperative treatment of heart failure and cardiogenic shock, including the intra-aortic balloon pump and a multitude of new inotropic agents and vasodilators, these do not supplant the need for operative intervention in these critically ill patients. This article describes the successful use of extracorporeal membrane oxygenation support as a bridge to recovery postoperatively in a patient with a large infarct-produced ventricular septal defect.

Although short-term mortality remains high in patients with postinfarction ventricular septal defects (VSDs), the long-term prognosis is promising for those who survive the first 30 days. Davies et al reported that, among 60 patients who survived surgical repair, the 5-, 10-, and 15-year survival rate was 69%, 50%, and 37%, respectively (1). While nonsurgical treatment of infarct-produced VSD has an early mortality of >90% (2), surgical repair may have better outcomes. Surgical closure of infarct-produced VSD in patients in cardiogenic shock is rarely described. Here we describe a case treated successfully with extracorporeal membrane oxygenation (ECMO) support as a bridge to recovery postoperatively in a patient with a large infarct-associated VSD.

CASE REPORT

A 69-year-old man with coronary artery disease presented with 6 days of substernal chest pain. At age 65, he underwent percutaneous coronary intervention of the left anterior descending coronary artery. On arrival at the emergency department, he was found to have an ST-elevation myocardial infarction. Cardiac catheterization revealed a completely occluded posterior descending artery, and it was stented. In the catheterization laboratory, the patient developed cardiogenic shock, and an intra-aortic balloon pump (IABP) was placed. A bedside echocardiogram revealed a VSD (Figure 1). The patient experienced cardiac arrest in the intensive care unit and was resuscitated with 10 minutes of cardiopulmonary resuscitation. At this point, peripherally cannulated venoarterial ECMO was initiated. In the following 24 hours, his liver and renal function deteriorated; surgery was deferred for another 24 hours to optimize liver and kidney function, and vasoactive and inotropic medications were reduced.

On day 3 of venoarterial ECMO, the VSD was operatively closed. The VSD, located posteriorly, was approximately 2 × 1 cm in diameter. It was repaired by a double patch technique.

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(Figure 2), with a pericardial patch reconstructing the septum and reducing the postrepair tension in the defect. A portion of the patch was secured on the left side of the ventricular septum, and the other portion of the patch was secured by pledgeted stitches. The left ventriculotomy was closed by a large ventricular patch, again using interrupted pledgeted stitches. The ECMO was converted to central cannulation to decrease tension on the pericardial patch by keeping the heart decompressed and was continued postoperatively.

On day 6 of venoarterial ECMO, the patient was on low-dose vasopressors and required a flow of 2.0 to 3.0 L. The patient was separated from ECMO, the chest was closed, and an IABP was kept in place. The patient returned to the intensive care unit with good biventricular function but required an increase in vasopressors. Nitric oxide and dobutamine were also needed to maintain hemodynamics. Over the next 4 days, the patient was weaned off nitric oxide and required lower doses of vasopressors. The IABP was removed. Within 7 days, the patient was completely weaned off vasopressors and inotropes. The patient spent 2 months in a rehabilitation facility and fully recovered, and he has continued to do well 18 months after surgery.

**DISCUSSION**

Postinfarction VSD repair remains a surgically challenging procedure with a high risk of mortality and morbidity (3, 4), partly due to the recurrence of VSD in 10% to 50% of cases (5–8). Better patient management over the years may have played a part in improving surgical results of postinfarction VSD. At our institution, the use of the double patch technique and ECMO support in the recovery period might have led to avoiding the recurrence of VSD, thus reducing hospital mortality. Therefore, this technique is to be recommended in the early repair of postinfarction VSD.

VSD operative mortality remains high. In a study by Pang et al (9), the 30-day operative mortality of postinfarction VSD was 40%, with an overall survival at 10 years near 50%. Birnbaum et al found that the mortality rate among patients with septal rupture who were treated conservatively without mechanical closure was approximately 24% in the first 24 hours, 46% at 1 week, and 67% to 82% at 2 months (10). Operative mortality depends on preoperative hemodynamics, which in turn depends on the degree of shunting and the extent of the acute infarct (11).
Park et al (2) studied 34 patients who underwent surgical repair of postinfarct VSD over 22 years in a single center, showing a 30-day mortality of 21% (7 patients), with profound cardiac failure as the cause of death. After 30 days, two patients died of sepsis and another died of subdural hemorrhage, resulting in an in-hospital mortality of 31%. The 5- and 10-year survival rates were 54% and 44%, respectively. These authors agreed that preoperative cardiogenic shock, systolic blood pressure, and right atrial pressure, along with cardiopulmonary bypass time, are major contributors to operative mortality. On the other hand, ejection fraction and the size of the intracardiac shunt were not determinants in postoperative outcome. Furthermore, the combination of elevated right atrial pressure with low systemic blood pressure was associated with an extremely poor prognosis (2, 10).

The ideal timing of VSD repair is a point for debate (Table 1) (2, 5, 9, 12–14). A few studies support our current strategy of delaying surgery, allowing optimization of medical management prior to intervention if permissible. Pang et al (9) found that only 2 of 38 patients remained sufficiently stable in New York Heart Association Class II to permit delayed surgery. Essentially, their study showed that delayed surgery only applied to a select group of patients who remain hemodynamically stable. An earlier study of 43 patients found that early surgical repair actually increased the survival rate (7). According to Gregoritic et al (15), the myocardial VSD edges are friable and the VSD enlarges during the first 10 days after acute myocardial infarction, so although waiting myocardial maturation is ideal it is not entirely possible.

The technique used to close the VSD also has importance; studies have shown that double patch techniques may decrease the incidence of residual shunt (9). In the study by Pang et al (9), the surgeons performed the single patch technique and had a 24% incidence of postoperative residual shunt. Utilizing viable myocardium and excluding the fragile infarcted myocardial tissue when suturing the pericardial patch also prevents recurrence (2). Concomitant coronary revascularization may prevent further risk of ischemic injury to the myocardium. While small VSDs may be repaired using percutaneous closure devices, large VSDs (20 × 15 mm), such as in the present case, should undergo immediate surgery, as they are prone to device embolization or residual defect. Contraindications to percutaneous device closure also include inappropriate anatomy to land the device and the location of the VSD (15).

Ventricular assist devices (VADs) have been shown to be beneficial in the setting of univentricular or biventricular failure. Typically VADs are used as a bridge to surgery or are placed postoperatively to allow for restoration of peripheral organ perfusion and provide recovery and maturation of the infarcted myocardium. By decreasing afterload and preload, VADs can help in providing rest for the myocardium. IABP placement can also be utilized to decrease afterload and increase coronary perfusion to the shocked myocardium. Blanche et al (16) found that postoperative use of an IABP reduces immediate postoperative mortality but does not improve long-term survival. Rohn et al (11) used venoarterial ECMO and an IABP to help stabilize a patient and surgically repair the VSD. Venoarterial ECMO was used as a VAD, allowing the patient to stabilize and improve clinically. On the third day, they were able to close the VSD, perform mitral valve plasty, and bypass the right coronary artery. The patient was doing well 6 months after surgery. Delayed surgery may be required to allow fibrous myocardial tissue growth and to prevent recurrence of VSD and dehiscence of the surgical patch. Percutaneous ECMO provides numerous benefits compared with placement of a conventional VAD. ECMO is economically efficient, prevents sternotomy, provides oxygenation support, and is easily reversible.

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<th>Late surgical intervention (N, %)</th>
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**Avocations**

![Pink tulip stamen. Photo by Rolando M. Solis, an interventional cardiologist at Baylor Scott and White Health Garland and The Heart Hospital Baylor Plano. He can be reached by e-mail at rmsolis@mac.com.](image)
A 19-year-old woman with a history of hydrocephalus treated at age 2 weeks with a ventriculoperitoneal shunt, last revised at age 15, presented to the emergency department with 2 weeks of diffuse abdominal pain and increasing girth and 2 days of right frontal headache relieved by lying supine. She initially had nausea and vomiting, which resolved after several days, leaving her with anorexia. There had been no fever or change in her bowel movements. Her blood pressure was 101/58 mm Hg, and her neurological examination was normal.

An abdominal ultrasound examination showed extensive ascites and normal ovaries and uterus. Computed tomography revealed a cystic accumulation of fluid in the lower abdomen. Because of a slow irregular pulse, an electrocardiogram was recorded and showed sinus bradycardia and arrhythmia with occasional junctional escape complexes (Figure).

At craniotomy, the proximal catheter from the fourth ventricular Dandy-Walker cyst was found to be obstructed and was replaced. The distal catheter was then replaced. Postoperatively, the patient’s abdominal pain resolved, and her headache decreased.

The Dandy-Walker deformity is a congenital malformation that occurs in approximately 1 in 20,000 newborns. Noncommunicating hydrocephalus is often part of the syndrome and is usually treated with ventriculoperitoneal shunting, as in this patient (1).

One hundred and fifteen years ago, Harvey Cushing, Dandy’s and Walker’s predecessor in neurosurgery at Johns Hopkins, described high blood pressure, bradycardia, and terminally a slow respiratory rate in patients with increased intracranial pressure, in the absence of high blood pressure this cannot be called Cushing’s phenomenon. In fact, no definite abnormality is noted in the electrocardiogram shown here. Sinus bradycardia and arrhythmia with occasional junctional escape complexes are not rare in healthy young adults. Also, the T-wave inversion in leads V1 to V3 is fairly common in normal young women.

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Diffuse large B-cell non-Hodgkin’s lymphoma and osteosclerotic myeloma with features of POEMS syndrome

Kyari Sumayin Ngamdu, MD, Alireza Torabi, MD, Nabeel Badri, MD, Mohammed Teleb, MD, and Sumit Gaur, MD

Multiple myeloma is a clonal hematopoietic neoplasm characterized by the proliferation of malignant plasma cells and associated end-organ damage, most notably lytic lesions in the bones. Osteosclerotic myeloma is an unusual variant of the disease in which the skeletal involvement is characterized by sclerotic lesions instead of classical lytic lesions. The disease can be associated with paraneoplastic symptoms, which have been given the acronym POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, M protein, skin changes). In addition to clonal plasma cell dyscrasias, some cases of POEMS syndrome are associated with Castleman’s disease, and in 11% to 30% of the cases both Castleman’s disease and clonal plasma cell proliferation are present. POEMS syndrome has rarely been described in patients with non-Hodgkin’s lymphoma.

POEMS syndrome usually occurs in patients with osteosclerotic myeloma or Castleman’s disease. We describe a patient with diffuse large B-cell non-Hodgkin’s lymphoma and osteosclerotic myeloma who developed features of POEMS syndrome.

CASE REPORT

In 2008, a 59-year-old Hispanic woman presented with fever, drenching night sweats, and a 15-pound weight loss over 6 weeks. She previously had hypothyroidism and hypertension. She had no other complaints and had no neurological symptoms. Examination showed bilateral cervical and left axillary adenopathy measuring up to 2 cm in size. Lymph nodes were nontender and freely mobile. The spleen was palpable 3 cm below the costal margin. Computed tomography (CT) scans showed 3-cm paraaortic lymph nodes and multiple foci of sclerotic bone lesions in the pelvis and spine. A skeletal survey confirmed extensive sclerotic lesions (Figure 1). The leukocyte count was 5600/μL with 68% neutrophils and 30% lymphocytes, the hemoglobin level was 11.8 g/dL, the platelet count was 320,000/μL, and creatinine and alanine aminotransferase were normal. Lactate dehydrogenase was elevated at 520 U/L. Serum immune electrophoresis showed a 2.1 g/dL monoclonal protein, which was IgG lambda on immunofixation. A 24-hour urine protein excretion showed 85 mg of protein, most of which was lambda light chains. An excisional biopsy of a lymph node showed sheets of large atypical lymphoid cells with vesicular chromatin and irregular nuclei with prominent nucleoli and frequent mitoses (Figure 2a). The lymphoid cells expressed CD-20, PAX 5, and BCL-6. They did not express CD-10 or BCL-2. The Ki-67 index was 90%. Immunohistochemical staining for kappa and lambda light chains showed polyclonal plasma cells and no staining of the malignant B cells. Polymerase chain reaction showed a clonal rearrangement of the immunoglobulin heavy chain gene. Bone marrow aspirate

Figure 1. A skeletal survey showing a large sclerotic lesion in the right iliac bone extending into the right acetabulum.

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showed normal trilineage hematopoiesis with no infiltration by lymphoma; the core biopsy showed sheets of atypical plasma cells in a fibrotic background and surrounding osteosclerosis (Figure 2b). Overall, 80% of the core was infiltrated by plasma cells that showed lambda light chain restriction.

The patient was diagnosed with stage III diffuse large B-cell lymphoma with an international prognostic index score of 2 and osteosclerotic myeloma. She then received six cycles of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone. At the end of chemotherapy, she had resolution of all palpable adenopathy and symptoms. She continued to have a palpable spleen, and serum electrophoresis continued to show a 2.1 g/dL of monoclonal IgG lambda. A free light chain assay showed a normal kappa: lambda ratio (0.84; normal, 0.26–1.65). CT/positron emission tomography (PET) scans showed no metabolically active lesions. Sclerotic bone lesions were noted and were not PET avid.

She was then started on bortezomib and dexamethasone. In addition, zoledronic acid was administered every 4 weeks. At the end of 4 months, her spleen size remained stable and serum immune electrophoresis showed a decline in M protein to 0.5 g/dL. She subsequently received maintenance therapy with lenalidomide (10 mg daily) for 2 years. At the end of 2 years, her M spike remained stable at 0.6 g/dL, PET showed no PET-avid sites, and peripheral blood counts and chemistries were normal. Lenalidomide was discontinued, and the patient was placed on surveillance and did well.

At age 66, in March 2015, the patient was noted to have bilateral nonpitting edema in her lower extremities extending up to her knees. Her spleen remained palpable 2 to 3 cm below the costal margin. Blood counts continued to show no cytopenias (white blood counts, 5200/μL; hemoglobin, 13.8 g/dL; and platelets, 380,000/μL), renal function was normal, and immunoelectrophoresis showed a stable M spike of 0.6 g/dL. A free light chain assay continued to show a normal kappa: lambda ratio (0.77). A 24-hour urine protein excretion showed 80 mg of protein, most of which was lambda light chains. A whole-body PET scan showed no signs of lymphoma relapse. A paraneoplastic phenomenon was suspected, and a plasma vascular endothelial growth factor (VEGF) level was noted to be elevated (1507 pg/mL; normal, 31–86 pg/mL). The patient was restarted on a regimen of bortezomib (1.3 mg/m²) and low-dose dexamethasone (20 mg weekly). Follow-up labs showed a decline in plasma VEGF levels, which correlated with resolution of her leg edema. Serum immune electrophoresis continued to show a stable M spike (Figure 3), and her spleen size did not regress with therapy.

**DISCUSSION**

POEMS syndrome is a paraneoplastic syndrome characterized by polyneuropathy, organomegaly, endocrinopathies, monoclonal protein, and skin changes. In addition, patients frequently have papilledema, extravascular volume overload (pleural effusions, ascites, peripheral edema), sclerotic bone lesions, and elevated plasma VEGF levels (1). Elevated circulating levels of various cytokines, including the plasma VEGF and
interleukin-6, contribute to the clinical manifestations of the syndrome (2–4). Unlike multiple myeloma, serial measurements of M spike in the serum or urine do not correlate with disease activity in POEMS syndrome. Measurements of plasma VEGF levels correlate with treatment response.

The association of POEMS syndrome with diffuse large B-cell lymphoma is rare. A PubMed literature search showed only one prior report of a patient who presented with primary cutaneous large B-cell lymphoma, leg type, and associated features of the POEMS syndrome (5). The lymphoma cells expressed VEGF and interleukin-6 by immunohistochemistry, suggesting that the malignant B cells were the source of the cytokines producing POEMS syndrome.

Our patient had many features suggestive of POEMS syndrome (monoclonal plasma cells in the bone marrow, sclerotic bone lesions, IgG lambda monoclonal protein, splenomegaly, and a relatively indolent course without any cytopenias, hypercalcemia, or renal insufficiency). She developed symptoms of fluid overload and elevated plasma VEGF levels 7 years after being treated for the lymphoma and at a time when she had no clinical or PET evidence of lymphoma relapse. In addition, she had clinical improvement and a decline in VEGF levels upon receiving therapy directed against the plasma cells. This suggests that unlike the first case, the malignant B cells were not the source of plasma VEGF elevation in our patient; the source was most likely the plasma cells or adjoining stroma.

The simultaneous diagnosis of osteosclerotic myeloma and diffuse large B-cell lymphoma in our patient raises the interesting question whether these two malignancies were clonally related. Immunohistochemical staining showed that the malignant lymphoma cells in our patient did not stain for lambda or kappa light chains, while the plasma cells were lambda restricted. Although not conclusive, this suggests that the two neoplasms might not be clonally related.

Diagnostic criteria have been proposed for POEMS syndrome (1). These require the mandatory presence of both polynuropathy and monoclonal plasma cell proliferation, in addition to other major and minor criteria to establish the diagnosis. Despite being exposed to neurotoxic drugs over the past 8 years (bortezomib, vincristine), our patient did not have any symptoms of polynuropathy. Yet, she had other unequivocal features of POEMS syndrome as described above. The other patient described by Nakayama et al did not have monoclonal plasma cell proliferation (5). Taken together, this suggests that POEMS syndrome may have an unusual presentation in patients with diffuse large B-cell lymphoma.

Hemoglobin SE disease was first described during the 1950s as a relatively benign microcytosis, but increasing prevalence has revealed a predisposition towards vasoocclusive sickling. Recognition of SE hemoglobinopathies’ potential complications is crucial so medical measures can be utilized to avoid multiorgan injury.

Microcytosis is a common finding on a peripheral blood smear that can reflect a variety of hematologic issues. We demonstrate the significance of identifying the etiology of a microcytosis by describing a patient whose underlying blood disorder resulted in multiorgan failure and death.

CASE PRESENTATION

A 52-year-old black woman with known chronic obstructive pulmonary disease, hepatitis C, and recurrent pulmonary embolism presented with a 3-day history of abdominal pain, chest discomfort, nonproductive cough, and dyspnea. Home medications included inhaled bronchodilators and rivaroxaban. Her blood pressure was 143/64 mm Hg; heart rate, 126 beats/minute; and respirations, 20 breaths/minute. Oxygen saturation was 91% on 5L nasal cannula. Her lungs were clear, and the physical exam was normal except for tenderness over the rectus abdominis. Laboratory results included normal electrolytes and liver enzymes but an elevated creatinine of 1.9 mg/dL and lactic acid of 3.2 mmol/L. Leukocytosis was present at 21 K/uL, with a platelet count of 122 K/uL. A microcytosis (68 fL) was noted with a hemoglobin of 13 g/dL. Chest radiograph and abdominal ultrasound disclosed cholelithiasis and a chronic right-sided pulmonary embolism. Broad-spectrum antibiotics, intravenous fluids, bronchodilators, and intravenous steroids were initiated.

Twelve hours later, the patient developed respiratory distress with coarse breath sounds. Blood gas after intubation revealed a pH of 7.43 and a partial pressure of oxygen of 58 (50% fraction of inspired oxygen). A repeat computed tomography scan did not show any new pulmonary emboli or infiltrates. Shortly afterwards, the patient entered pulseless electrical activity but recovered after cardiopulmonary resuscitation. Her hemoglobin rapidly decreased to 6 g/dL, requiring packed red blood cell support without any gross evidence of bleeding. The prothrombin and partial prothrombin time were normal with a fibrinogen level of 281 mg/dL. The patient required multiple vasopressors and continuous renal replacement therapy for worsening hyperkalemia. All cultures remained negative, and the patient went into asystole 26 hours after admission. Laboratory values revealed a hemoglobin of 11.8 g/dL and 1+ schistocytes but no sickled erythrocytes. Iron studies disclosed a serum iron level of 50 μg/dL, total iron binding capacity of 294 μg/dL, and ferritin level of 50 ng/mL.

At autopsy, the pulmonary hilar and peripheral arteries were free of grossly apparent thromboemboli. On microscopic examination, the alveolar septal capillaries were congested, with small and larger vessels packed with sickled erythrocytes (Figure 1). In addition, sickled erythrocyte congestion was seen in the pituitary gland, liver, spleen, colon, stomach, and urinary system (Figure 1). Hemoglobin electrophoresis revealed 8% hemoglobin E, 25% hemoglobin S, 64% hemoglobin A, and 3% hemoglobin A2, consistent with a transfused patient with hemoglobin SE disease. It was concluded that this 52-year-old woman died of a cardiac arrhythmia secondary to chronic lung disease and vasoocclusion with intravascular ischemia.

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<td>Lactic acid (mmol/L)</td>
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<td>3.2</td>
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From the Department of Internal Medicine (Smith), Department of Hematology and Oncology (Cooper), Department of Forensic Pathology (Guileyardo), and Division of Pulmonology and Critical Care (Mora), Baylor University Medical Center at Dallas.

Corresponding author: Avery Smith, MD, Department of Internal Medicine, Baylor University Medical Center at Dallas, 3500 Gaston Avenue, Dallas, TX 75246 (e-mail: Avery.Smith@baylorhealth.edu).
DISCUSSION

Microcytic anemia is based on having a mean corpuscular volume < 80 fL. Small erythrocytes are primarily related to abnormalities in the production of globin or the heme components of hemoglobin. This can result from iron deficiency, chronic inflammation, iron-resistant iron deficiency anemia, and sideroblastic anemia alpha/beta thalassemia (1). Thus, the differential for microcytosis is broad, but expansion is essential to include variant hemoglobinopathies.

Two of the world’s most common variant hemoglobins are hemoglobin S and hemoglobin E. The amino acid substitution of glutamine for valine in the beta chain resulting in hemoglobin S is most prevalent in people of African, Caribbean, and South American descent. In contrast, the mutation in which lysine is substituted for glutamine at position 26 of the beta chain results in hemoglobin E (2). It is most common in the “hemoglobin E triangle” of Cambodia, Laos, and Thailand but is also present in the remainder of Southeast Asia. Patients who are homozygotes or heterozygotes for hemoglobin E are typically asymptomatic. Typical hemoglobin levels range from 10.5 to 12 g/dL, while mean corpuscular volumes range from 65 to 80 fL. The evolution of these hemoglobinopathies stems from resistance against malarial disease (3). Despite the geographical dissimilarities, population migrations and interracial relationships have resulted in the emergence of SE hemoglobinopathy. The first case was described in Turkey during 1957, but an increasing incidence of the disease has been documented (4). Hemoglobin electrophoresis demonstrates a hemoglobin S level of 62% ± 7% and a hemoglobin E level of 33% ± 4% (4). Although SE hemoglobinopathy is considered relatively benign, retrospective studies have revealed that patients with it develop complications of vasoocclusive sickling, including acute pain syndromes, avascular necrosis of long bones, splenic infarction, and sickle cell retinopathy (5).

Our patient presented with acute pain symptoms and microcytosis despite the absence of anemia. Iron studies did not suggest iron deficiency. The patient’s acute respiratory failure and hypoxia initiated her vasoocclusive sickling, which was demonstrated by sickled erythrocyte congestion in the lungs, liver, spleen, colon, stomach, and urinary system. The presence of microscopic pulmonary capillary obstruction due to sickle crisis explains the patient’s imminent hypoxia and repeated cardiac arrests. Thus, recognition of SE disease’s potential complications is crucial so that exchange transfusions can be utilized to avoid the risk of multiorgan injury.

A case of erythropoietic protoporphyria

Kathryn Lindsey, MD, Micah Burch, MD, and John R. Krause, MD

A 53-year-old Texas rancher developed a blistering skin rash that was sensitive to exposure to sunlight. He was referred to hematology with a presumptive diagnosis of porphyria. His peripheral blood counts were within normal limits, and a bone marrow examination revealed erythroid dyspoiesis and ringed sideroblasts. Serum, plasma, and erythrocyte protoporphyrin levels were elevated, the findings of which are consistent with a diagnosis of erythropoietic protoporphyria. This paper discusses the diagnosis and etiology of the porphyrias.

CASE REPORT

A 53-year-old rancher from South Texas presented to his primary care physician with a blistering skin rash. He noted that his rash was predominantly on unclothed skin surfaces, namely his face and arms. The rash was very painful and seemed to be worsened by exposure to sunlight. Prior to this presentation he had been in very good health, with no diagnosed chronic conditions. He was evaluated initially by dermatology. In addition to the photosensitive skin rash, he was found to have a mild anemia. His blood counts included a hemoglobin of 11.4 g/dL, hematocrit of 32.2%, white blood cell count of 4.8 K/μL, and platelet count of 160 K/μL. The differential count was normal. He was referred to hematology with a presumptive diagnosis of new-onset porphyria. A bone marrow biopsy was performed.

The peripheral blood smear was unremarkable. The bone marrow aspirate and trephine biopsy showed trilineage hypercellularity (Figure 1a). Dyspoietic features were noted in the erythroid and megakaryocytic lineages in the form of irregular nuclear features and nuclear to cytoplasmic dyssynchrony. A Prussian blue stain performed on an aspirate smear was remarkable for numerous ring sideroblasts (Figure 1b). The ancillary studies revealed no specific pathology. Flow cytometry found no evidence of a lymphoproliferative or myeloproliferative disease. Conventional cytogenetics grew a normal complement of chromosomes. Fluorescence in situ hybridization for common myelodysplasia alterations highlighted normal patterns.

Because of the clinical suspicion and the pathologic findings of erythroid dyspoiesis and ring sideroblasts, a peripheral blood sample was sent for testing of protoporphyrin levels. The total plasma porphyrins were 46.9 μg/dL (reference range, <1.0), total serum porphyrins were 784 nmol/L (reference range, 0–15), erythrocyte protoporphyrins were 300 umol/mol heme (reference range, <70), and the fractionation of plasma porphyrins (emission spectrum) was at a wave length suggestive of erythropoietic protoporphyria (EPP). With the positive results, he was considered to have EPP secondary to a myelodysplastic syndrome, refractory anemia with ring sideroblasts.

The patient’s peripheral blood was sent for sequencing of his ferrochelatase gene, which showed a c.913G>T change in exon 9 which altered the canonical splice site and was therefore predicted to be deleterious. His skin disease has been well controlled with Lumitene, a high-dose beta-carotene supplement, and sun avoidance. The patient has been monitored with complete blood counts.

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and metabolic profiles every 2 to 3 months since diagnosis and has required no other treatment. His liver enzymes have been normal except for bilirubin, which has mildly risen to 2.2 mg/dL. A bone marrow transplant is planned.

DISCUSSION

The porphyrias are a collection of diseases caused by inborn and acquired errors of heme synthesis. Heme is necessary for several types of hemoproteins, including liver and respiratory cytochromes, but hemoglobin synthesis for red blood cells accounts for the vast majority of heme synthesis in humans. The synthesis of the heme molecule, a heterocyclic organic ring surrounding an iron ion, is catalyzed in eight steps from succinyl coenzyme A and glycine (Figure 2). These eight enzymes are encoded on nine different genes, each with described mutations. Two genes encode isoenzymes that catalyze the first step in the pathway; one is erythroid specific, aminolevulinic acid synthase 2 (ALAS2). A loss of function mutation at any step marks a stop in the synthetic pathway and an accumulation of precursor molecules. These precursors have no physiologic function, are not normally detected at significant levels, and are toxic to varying degrees. Tight regulatory control is necessary and is cell type specific. In erythroid precursors, iron availability is required for the translation of the ALAS2 mRNA. The eighth step is also iron dependent, as ferrochelatase must add an iron ion to each protoporphyrin. In the liver, heme itself represses the translation of the first and rate-limiting enzyme, ALAS1 (1).

Except in rare cases, EPP is an inherited form of ferrochelatase deficiency or malfunction or an erythroid-specific ALAS2 enzyme gain of function mutation (Figure 2). The genetics of these diseases are complex, with forms with low penetrance and late onset. Acquired forms of EPP are caused by somatic mutations of the ferrochelatase gene often associated with the genetic instability of an erythroid precursors in erythrocytes and plasma and are exposed to light. Absorbing light at 320 to 595 nm, protoporphyrin is excited to a triplet state. The energy transfer is propagated to oxygen, resulting in reactive oxygen species. The pathogenic consequence is oxidative damage of proteins, lipids, and nucleic acids. Among its effects, this phenomenon can activate complement and degranulate mast cells. The histopathologic findings are consistent with the cycle of damage and repair. The blood vessels of the basal lamina thicken with perivascular hyaline material and proliferate for the sake of perfusion (2).

The liver is tasked with the excretion of the excess protoporphyrins. If its capacity is overwhelmed, the protoporphyrins are deposited in hepatocytes. Birefringent crystals, characterized by Maltese cross shapes, are visible within the deposits. The liver reacts as it would to any chronic insult with regeneration and fibrosis potentially leading to cirrhosis (2). The conventional histologic bone marrow pathology is not as striking. Increased ring sideroblasts by light microscopy have been described, but in a greater number of cases there is ultrastructural evidence of iron deposition in the mitochondria of erythroblasts (4). In acquired forms of the disease, the apparent histopathology will be that of the underlying myelodysplastic or myeloproliferative disease. A microcytic anemia may be seen in the inherited X-linked dominant EPP with decreases in iron stores and hemoglobin (5).

The laboratory investigation of EPP requires finding elevated protoporphyrins in erythrocytes, plasma, and feces, as in this case. Protoporphyrins are not excreted in urine. Protoporphyrins are exquisitely light sensitive. Since plasma concentrations fall rapidly upon exposure to light, measurement of erythrocyte protoporphyrin is usually preferred (6).


Figure 2. Heme synthesis.
Lactate levels with glioblastoma multiforme

Arunpreet Singh Kahlon, MBBS, Mariam Alexander, MD, Arundeepl Kahlon, MD, and Jonathan Wright, MD

A 37-year-old woman with known glioblastoma multiforme was admitted for treatment of new deep vein thrombosis. Anion gap and plasma lactate levels were found to be elevated. Magnetic resonance imaging of the brain showed a stable, advanced glioblastoma multiforme. All causes of lactic acidosis, including infections and medications, were ruled out. Aggressive tumors have been shown to produce lactate levels in minute quantities in their microenvironment, which helps them metastasize and evade immune response and even radiation.

Malignancy is a known cause of elevated lactate, although it is rarely recognized in nonhematologic cancers. We present a case of chronically elevated lactate levels in a patient with glioblastoma multiforme (GBM), a circumstance not reported previously.

CASE DESCRIPTION

A 37-year-old woman with GBM and a history of ventriculoperitoneal shunt, obesity, and glucocorticoid-induced diabetes mellitus was admitted for treatment of newly found deep vein thrombosis in her right leg. Except for leg swelling, the patient was asymptomatic. An anion gap of 20 was found, but her serum bicarbonate level was 25 mmol/L. The plasma lactate level was 5.5 mmol/L and ketones were negative. The blood urea nitrogen was 17 mg/dL and creatinine was 1 mg/dL. Liver function tests were also within normal limits. An arterial blood gas revealed a pH of 7.40, partial pressure of carbon dioxide of 42 mm Hg, oxygen saturation of 99%, bicarbonate level of 27 mmol/L, base excess of 1, and partial pressure of oxygen of 100 mm Hg on 2 L oxygen by nasal cannula. Her anion gap had been elevated for approximately a year. During the entire time her serum bicarbonate levels were within normal range. Serial lactate levels and arterial blood gas during the same hospital admission revealed persistently elevated lactate levels. Magnetic resonance (MR) imaging of the brain revealed the glioblastoma to be stable compared with prior imaging (Figure). She was not receiving chemotherapy for GBM due to the advanced stage of her disease; her treatment consisted of dexamethasone, acetaminophen/oxycodone, and newly started low-molecular-weight heparin for deep vein thrombosis. She died from her GBM.

DISCUSSION

High lactate levels in malignancies are associated with poor prognosis (1). The pathogenesis of lactate production in tumor cells is not well understood (2). Tumorigenesis leads to alteration of metabolic switch in genes regulating glycolysis, such as PI3K, mTOR, KRAS, EGF, and HIF-1α, causing increased glucose uptake and lactate formation by cancer cells (1). This is caused by aerobic glycolysis or the Warburg effect. In 1925, Warburg showed that blood in veins from tumors had more lactate than the arteries feeding them (3) independent of glucose

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uptake or hypoxia (4). Several oncogenes and tumor suppressor genes are involved in the switch from oxidative phosphorylation to glycolysis. The phosphoinositide-3-kinase (PI3K)/AKT genetic pathway, which is a proto-oncogene, promotes the switch from oxidative phosphorylation to glycolysis. Similarly, antioncogenes such as p53/TIGAR have been shown to inhibit the Warburg effect, thus preventing tumor progression (5). Studies are investigating the role of PI3K-Akt-mTOR inhibitors as treatment for GBM (6). Although the Warburg effect is most commonly seen in hematologic malignancies, it has also been observed in solid malignancies (7).

Lactate is a powerful signaling molecule in tumor cells and has been shown to promote cell motility (8) and enhance cell migration (9). Increased lactate levels can induce resistance to radiation and chemotherapy (10). This resistance results from the antioxidant properties of lactate, which neutralize reactive oxygen species produced by ionizing radiation to induce DNA/RNA damage to tumor cells. Lactate also promotes tumor angiogenesis by inducing expression of vascular endothelial growth factor (11). In mouse models, intraperitoneal injections of lactate were able to increase metastasis and vascularity in the mouse microenvironment, which is associated with poor survival and advanced disease (15). The case discussed above describes an unusual picture of chronically elevated lactate without acidosis. All hypoxic and nonhypoxic causes of elevated lactate levels were eliminated, suggesting that the elevation was likely due to GBM. GBM cell lines have also been shown to overexpress lactate dehydrogenase A (LDHA), which is required for anaerobic glycolysis in normal cells but increases lactate production and the rate of glycolysis through the Warburg effect in cancer cells (16). Inhibition of LDHA promotes apoptosis, decreases cell growth, migration, and invasion, and is currently being investigated as a potential therapeutic target (17). More research is required to establish the role of LDHA in normal brain cells before such targets can be further investigated in GBM. Studies correlating MR spectroscopy and blood lactate levels in a cohort of GBM patients are needed to determine if LDHA can be used as a marker for tumor progression, prognosis, and response to therapy.

Dermatofibrosarcoma protuberans (DFSP) is a rare cutaneous tumor with a tendency towards local recurrence. A 26-year-old woman presented with a 3 × 2 cm raised, purple-hued lesion on her left breast. Excisional biopsy identified the lesion as a DFSP. She underwent two additional operations to achieve widely clear margins. Operative excision is the primary treatment of dermatofibrosarcoma protuberans of the breast.

Dermatofibrosarcoma protuberans (DFSP) is a rare, locally aggressive cutaneous tumor. It is characterized by its slow, infiltrative growth and marked tendency towards local recurrence after surgical resection (1). The incidence rate is 4.2 to 4.5 cases per million persons per year in the United States (2). The most common location of DFSP is the trunk, with 25% of cases affecting the chest and shoulder areas (1). At least 40 case reports of DFSP in the breast have been reported, but less than half address the surgical management (3–17), which we describe here.

CASE DESCRIPTION
A 26-year-old Hispanic woman presented to the surgery clinic at Baylor University Medical Center at Dallas complaining of a left breast lesion. The lesion had been present since an incision and drainage procedure in the area approximately 8 years earlier. She noted that it had slowly grown over this period. The lesion was approximately 2 × 3 cm in size. It was located 5 cm from the nipple at the 7 o’clock position on the left breast. The lesion had a keloid-like appearance in that it was purple-hued, protuberant, and irregular. She had no ulceration of the lesion or nipple discharge. She was not taking any hormone therapy. There was no family history of breast, ovarian, skin, or other cancers. An ultrasound revealed a 3 cm lesion of the dermis corresponding with the area of concern.

An excisional biopsy of the lesion with gross margins using a radially oriented elliptical incision disclosed it to be DFSP (Figure 1). The lesion had a low mitotic index, but there was invasion into the underlying adipose tissue. All margins were positive for residual disease. She subsequently had wide local excision with a 2 cm margin of tissue taken circumferentially around the previous incision. Initial frozen section evaluation revealed that the deep margin was positive, so a new margin was taken. Frozen section analysis of the new margin was negative at the time of surgery, but on final analysis DFSP was seen at the lateral edge and another focus 2 mm away from the new deep margin. The patient underwent a third operation for wide local excision, again with 2 cm circumferential margins. All margins were clear by at least 1 cm on histological evaluation. The patient has done well postoperatively with a satisfactory cosmetic result (Figure 2).
**DISCUSSION**

DFSP is known to have a high rate of recurrence after surgical excision. The propensity for this tumor to develop subclinical, tentacle-like extensions of tumor cells into the underlying deep tissue makes complete excision difficult. Prior to the 1980s, recurrence rates for DFSP after local excision ranged from 10% to 60%. Pooled data from the last 20 years reveal that the local recurrence rate now ranges from 0% to 21%, with more recent studies advocating the use of wide surgical margins (18). “Wide local excision,” however, has not been well defined. The National Comprehensive Cancer Network guidelines recommend excision of DFSP with 2 to 4 cm margins including the deep investing fascia of muscle, which is in line with recommendations for sarcomas in general. Data from the application of Mohs surgery for DFSP have shown that 75% of tumors are cleared with 1 cm margins, 80% with 1.5 cm margins, 85% with 2 cm margins, and 95% with 2.5 cm margins. Tumors that were <2 cm are usually cleared with a 1.5 cm margin, while 2.5 cm is required to clear tumors >2 cm (19).

While it would be ideal to capture all tissue down through the investing fascia of the muscle, this might not be practical in every case of DFSP of the breast. Given that the breast is a unique area of the body where intervening tissue lies between the subcutaneous adipose tissue and the underlying muscle fascia, this begs the question as to whether the additional tissue resection is necessary. In our case, approximately 4 cm of deep margin was excised without encountering the fascia of the pectoralis major, and a negative margin was accepted as an adequate wide local excision.

The optimal surgical treatment to achieve negative margins can be variable based on tumor size and location on the breast. A review of the literature revealed a variety of surgical approaches to address DFSP of the breast. One patient underwent a mastectomy, one patient underwent a wide local excision with concomitant breast reduction, three patients underwent a wide local excision with flap reconstruction, one patient underwent a wide local excision with skin graft, and nine patients underwent wide local excision with primary closure (Table 1). The reconstructive challenge in DFSP of the breast is to balance the oncologic principles of adequate resection with the cosmetic goals of acceptable symmetry and contour. In our case, we were able to achieve adequate cosmetic results with a wide local excision and primary closure, but this might not be feasible in all patients. The National Comprehensive Cancer Network recommends that any reconstruction that involves extensive undermining or tissue movement should be delayed until histologic margins are verified (2). Due to the inaccuracy of intraoperative pathologic assessments with frozen section, staged reconstruction should be considered.

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<th>Age (yr)</th>
<th>Size of lesion (cm)</th>
<th>Recurrence or primary</th>
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<th>Margin size (cm)</th>
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Avocations

Fort of San Juan de Ulua built in the 14th century, Veracruz, Veracruz, Mexico. Photo by Alejandro C. Arroliga, MD. Dr. Arroliga is chairman of the Scott and White Clinic Board of Directors and can be reached at Alejandro.Arroliga@BSWHealth.org.
We describe a 23-year-old white man who presented with anasarca and a new periumbilical mass. He had preserved kidney function and laboratory findings consistent with nephrotic syndrome, including 9.7 g/day albuminuria. Serum serologies were positive for anti-SSa and anti-SSb and low complements but were negative for antinuclear antibody. Pathologic findings of the abdominal mass showed a mammary-type myofibroblastoma. A kidney biopsy revealed a diffuse proliferative and membranous immune-mediated glomerulonephritis with 10% interstitial fibrosis. This is a novel case of mammary-type myofibroblastoma associated with nephrotic syndrome mimicking a proliferative lupus pattern.

Nephrotic syndrome (NS) involves a constellation of physical and laboratory findings, including urinary albumin excretion >3.5 g/day, hypoalbuminemia, hyperlipidemia, and peripheral edema (1). Paraneoplastic glomerulopathy has previously been described as a common cause of NS, with most glomerular lesions having a membranous pattern (2). A minority of patients have proliferative lesions that can mimic lupus nephritis. We describe a young man who did not have systemic lupus erythematosus (SLE) but had glomerular findings of SLE-like lesions after a new diagnosis of a rare abdominal myofibroblastoma.

CASE DESCRIPTION

A 23-year-old white railroad conductor presented with dyspnea and progressive edema spreading from his feet to his abdomen over several days. He noted having fatigue, night sweats, headache, dyspnea, cough, and a 60-pound weight loss over 6 months. Two months earlier, he was seen in the emergency department with abdominal pain. Computed tomography (CT) revealed diffuse lymphadenopathy and an edematous process in the extraperitoneal region of the pelvis anterior to the bladder. He was started on prednisone 20 mg daily for 4 weeks and told to follow up with oncology.

On exam his vital signs were stable, except for a blood pressure of 160/95 mm Hg. He had mild crackles at both lung bases and a tender 4 cm palpable periumbilical mass. He had +4 pedal edema and no rash. Pertinent laboratory results included a white blood cell count of 6400/μL; hemoglobin, 8.3 g/dL; hematocrit, 26.1%; mean corpuscular volume, 77.7 fL; albumin, 1.3 g/dL; triglycerides, 263 mg/dL; low-density lipoprotein cholesterol, 121 mg/dL; and brain natriuretic peptide, 16 pg/mL. Urinalysis revealed a specific gravity of 1.027, pH of 6.0, 4+ protein, 3+ blood, 50 to 100 red blood cells per high-power field, 10 to 15 white blood cells per high-power field, and 9.7 g/day of albuminuria. Serum serologies returned low C3, 51.9 mg/dL; low C4, 8.9 mg/dL; positive anti-SS-A/Ro, anti-SS-B/La. Urine protein electrophoresis was 1144 mg/dL without M-spike. His entire serologic workup was negative including antinuclear antibody twice and anti-DNA. An abdominal CT scan revealed a mass (Figure 1). Colonoscopy and esophagogastroduodenoscopy were unremarkable.

Figure 1. CT showing a focal hypodensity extending from the anterior aspect of the pelvis into the lower anterior abdomen, with the largest low-density lobular region just deep to the abdominal wall in the lower anterior abdomen measuring up to 9 × 4.7 cm (arrow).
A kidney biopsy revealed diffuse proliferative and membranous immune-mediated glomerulonephritis with 10% interstitial fibrosis and cellular crescents but no vascular disease. Immunofluorescence staining revealed a diffuse fine granular pattern in the capillary loops and mesangium for IgG (2 to 3+), IgM (1 to 2+), kappa (2 to 3+), and lambda light chains (2 to 3+), but was negative for IgA (Figure 2). An excisional biopsy of the pelvic mass revealed a lipomatous neoplasm with prominent myxoid areas. Molecular testing with fluorescence in situ hybridization was negative for DDIT3, which did not support myxoid liposarcoma.

The patient was treated for possible renal-limited lupus nephritis given his proliferative lesions with crescents. He was diuresed with furosemide and started on the Aspreva Lupus Management Study Group trial induction regimen in order to avoid gonadotoxicity with cyclophosphamide (3). The patient returned 2 weeks later with a continued complaint of dyspnea. His labs showed preserved renal function with persistent hypoalbuminemia. Serum C3 and C4 labs had increased to 89 mg/dL and 25.2 mg/dL, respectively, and 24-hour urine albumin was higher at 26 g/day. Because of his worsening albuminuria, he was given rituximab based on the LUNAR study protocol (4). The abdominal mass was surgically removed, and pathology revealed a cellular spindle cell neoplasm suggestive of mammary-type myofibroblastoma. One month later, his 24-hour urine albumin had fallen markedly to 1.5 g/day.

**DISCUSSION**

NS is caused by primary glomerular disease or is a consequence of a systemic disease or pathologic condition. Paraneoplastic glomerulopathy attributes the manifestations of glomerulonephritis not to tumor invasion or metastasis, but to unknown hormones, cytokines, or tumor antigens from the malignancy (2). NS is usually treated with guideline-based therapy for malignancy eradication (5, 6).

Our patient was diagnosed with a relatively rare tumor, mammary-type myofibroblastoma. This tumor is considered benign and does well even when the margins of resection are positive. It usually comprises bland spindle cells intermixed with collagen bundles and adipocytes. About 90% of these tumors express CD34 and desmin. Genetically, 92% of patients have a deletion or rearrangement of 13q14 resulting in a loss of the retinoblastoma gene. Originally, mammary-type myofibroblastoma was described in the male breast (7), but subsequently it has been described in other anatomic sites. In their 2015 review, Howitt and Fletcher described 143 cases, and only one
case had spread (8). There are no reports of this tumor being associated with NS.

The patient presented at the unusually young age of 23, while most malignancies associated with NS are in older patients (2). The kidney biopsy was consistent with a membranous pattern with subepithelial deposits on electron microscopy, but also with a proliferative pattern including crescents, which appeared lupus like. The patient did not have classic SLE clinicopathologic symptoms, with two negative antinuclear antibody tests and a negative anti-DNA test. Some patients present with histologic findings of SLE nephritis on biopsy, but without extrarenal symptoms, as described in a case series by Huerta et al (9). Without specific guidelines for treatment, patients with this presentation are treated as if they have true SLE nephritis, because most will eventually develop extrarenal SLE (9).

We surmised that this patient had a benign mammary-type myofibroblastoma that caused the proliferative glomerulopathy, and the NS resolved either by removal of this tumor or rituximab infusion. This case describes the first published association of mammary-type myofibroblastoma and NS.

Mammary myofibroblastomas are rare benign stromal cell tumors that can occur in both men and women. With the prevalence of screening mammography, these neoplasms are now being detected at smaller sizes. However, patients, especially men, can present with a palpable mass where screening mammography is not routinely performed. This case highlights the clinical presentation, imaging appearances, and pathologic features of this rare benign neoplasm.

CASE REPORT

A 57-year-old man presented with a right breast mass that had been slowly increasing in size over the past 5 years. He denied a personal or family history of cancer. The mass was firm, mobile, nontender, and involved the entire right breast. It measured approximately 10 cm in greatest diameter. There was no skin erythema, nipple retraction, or nipple discharge. No axillary or supraclavicular adenopathy was palpated. A mammogram disclosed an oval mass with circumscribed margins measuring up to 10 cm and occupying most of the right breast (Figure 1a,1b). Ultrasound demonstrated an oval, solid mass with circumscribed margins measuring 10 cm. The echotexture of the mass was heterogeneous (Figure 1c). Internal vascularity was noted on color Doppler imaging, confirming the solid nature of the mass. A survey ultrasound of the axilla detected no abnormal axillary lymph nodes. Percutaneous biopsy under ultrasound guidance yielded four 14-gauge core specimens, which on histopathologic diagnosis revealed mammary myofibroblastoma.

The patient was subsequently referred to a breast surgeon for excision. Using a bat wing excision, the subcutaneous tissue
was dissected using electrocautery. The mass was removed intact with blunt dissection. An intraoperative specimen radiograph confirmed excision of the mass and biopsy clip. The deep dermis and skin were subsequently closed. The excised mass measured 11.0 × 9.2 × 6.5 cm and weighed 279 g. On cut section, the mass was well circumscribed, tan-white to yellow-tan, firm, nodular, and homogenous, with no areas of hemorrhage, necrosis, overt calcium, or cystic degeneration (Figure 2a). The mass consisted of uniformly cellular, basal spindle cells arranged in short and long fascicles and an occasional storiform pattern, with interspersed thick and thin collagen fibers (Figure 2b). No area of necrosis or infiltration into the surrounding breast parenchyma was noted. The spindle cells showed a low nuclear to cytoplasmic ratio, moderate eosinophilic to amphophilic cytoplasm, and elongated nuclei with blunted ends (Figure 2c). Rare mitotic figures were noted.

Based on cytomorphology, immunohistochemical analysis excluded spindle cell metaplastic carcinoma and metastatic melanoma. The spindle cells were strongly and diffusely positive with CD34, smooth muscle actin, desmin, estrogen receptor, and progesterone receptor immunostains, compatible with the diagnosis of mammary myofibroblastoma. The tumor cells were negative for pan-cytokeratin AE1/AE3 and S100, excluding spindle cell metaplastic carcinoma and spindle cell melanoma, respectively.

**DISCUSSION**

First reported by Toker in 1981 (1) and first named by Wargotz in 1987 (2), mammary myofibroblastoma is a mesenchymal neoplasm derived from stromal fibroblasts. Although myofibroblastomas have been reported in extramammary locations, they are most commonly found within the breast parenchyma. These masses are termed myofibroblasts because they are considered to be fibroblastic cells that show smooth muscle differentiation since they express desmin and actin (smooth muscle markers). When in the breast, this benign lesion usually presents as a firm and mobile mass. Typically, it is unilateral, painless, and may steadily increase in size. It can reach large dimensions, as in this case, but usually ranges from 1 to 4 cm. The demographic distribution of myofibroblastoma of the breast occurs with equal prevalence, predominantly in older men and women with a median age of presentation of 55 years (3). Often, this mass will present a diagnostic dilemma both on imaging and clinically, as its features may overlap with those of other benign and sometimes malignant lesions.

The imaging features of mammary myofibroblastoma are nonspecific. Consequently, these lesions are hard to characterize as definitely benign or malignant, prompting the need for biopsy. With the widespread use of screening mammography, many lesions may be detected at small sizes (approximately 1 cm). The lesion typically appears as a well-circumscribed oval or round high-density mass on mammography. Architectural distortion and calcium are not typical features of this benign neoplasm (4). Sonographically, the mass usually presents as an oval, circumscribed hypoechoic solid mass. Its echogenicity, however, can be hyperechoic, and posterior acoustic shadowing may be present (4). On magnetic resonance imaging, these lesions typically enhance and can demonstrate internal septations on T2-weighted images (5). Myofibroblastomas are typically surgically excised with a good prognosis.

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A 69-year-old white man presented with several episodes of hematochezia. Colonoscopy demonstrated multiple colonic blebs localized mainly in the distal transverse colon. Esophagogastrroduodenoscopy, capsule endoscopy, and computed tomography of the abdomen did not reveal any abnormalities. The patient required several blood transfusions and eventually required a subtotal colectomy with ileosigmoid anastomosis for definitive bleeding control. Pathology was remarkable for multifocal vascular ectasia, consistent with the diagnosis of blue rubber bleb nevus syndrome.

Blue rubber bleb nevus syndrome is a rare disorder characterized by cutaneous and gastrointestinal vascular malformations that was originally described in 1860 and 1958 by Gascoyen (1) and Bean (2), respectively. Clinically, most patients present with symptoms related to iron-deficiency anemia. Rarely, patients can experience overt gastrointestinal bleeding resulting in significant transfusion requirements (3). The incidence of blue rubber bleb nevus syndrome is very low, with approximately 200 cases reported in the literature, mostly described in children and young adults (4).

CASE REPORT

A 69-year-old white man presented after multiple episodes of bright red blood per rectum that required several blood transfusions. He denied a previous history of skin lesions or a family history of similar symptoms. He had no skin lesions. Esophagogastrroduodenoscopy was normal. Colonoscopy showed diffuse colonic blebs mostly localized to the distal transverse colon (Figure 1). A computed tomography scan, small bowel series, and video-capsule small bowel study were normal. The patient continued to have intermittent bleeding associated with a decreasing hemoglobin level. A subtotal colectomy with ileosigmoid anastomosis was performed (Figure 2). Histological sections showed multifocal thin-walled vascular ectasia with associated mucosal erosion/ulcerations and hemorrhage predominantly involving the mucosa and submucosa of the entire colon (Figure 3). The histologic, immunohistochemical, and special stain findings were compatible with the venous malformations seen in blue rubber bleb nevus syndrome. The patient recovered well and was discharged home on postoperative day 7. At 1-year follow-up, he reported no additional episodes of bleeding.

DISCUSSION

This case illustrates an atypical presentation of lower gastrointestinal bleeding from localized blue rubber bleb nevus syndrome, a rare vascular anomaly of unknown etiology characterized by multifocal venous malformations of the skin, soft tissues, and gastrointestinal tract. This syndrome most commonly occurs sporadically but can be associated with an autosomal dominant inheritance (5). The skin lesions usually present at birth and the gastrointestinal lesions present at a later age but continue throughout life. The lesions can occur anywhere in the gastrointestinal tract and cause severe bleeding that can lead to death.

Management of this condition is directed towards control of bleeding, repletion of iron stores, and blood transfusions when there is significant bleeding. It is important to evaluate the entire gastrointestinal tract via esophagogastrroduodenoscopy and a video-capsule small bowel study to look for synchronous lesions. Several antiangiogenic agents, including octreotide, interferon alpha, and corticosteroids, have been studied to reduce the frequency and severity of bleeding episodes. These small studies lack long-term prospective data and suggest that lesions recur after discontinuation of therapy (6, 7). Low-dose sirolimus (8) was reported to be effective in one pediatric patient with recurrent gastrointestinal bleeding episodes despite conservative management. Endoscopic approaches for control of bleeding include laser photocoagulation, sclerosis, band ligation, and polypectomy (9, 10). Lastly, surgery has been advocated as definitive treatment for gastrointestinal bleeding that does not respond to the aforementioned strategies. The largest prospective series comes from the pediatric surgery literature, which reports effective use of a wedge resection, polypectomy.
suture ligation, segmental bowel resection, and band ligation with effective control of bleeding. Ten patients were followed for a mean of 5 years, with only one of the patients experiencing recurrent gastrointestinal bleeding (11).

Amphetamine-related ischemic colitis causing gastrointestinal bleeding

Ragesh Panikkath, MD, and Deepa Panikkath, MD

A 43-year-old woman presented with acute lower intestinal bleeding requiring blood transfusion. Multiple initial investigations did not reveal the cause of the bleeding.Colonoscopy performed 2 days later showed features suggestive of ischemic colitis. On detailed history, the patient admitted to using amphetamines, and her urine drug screen was positive for them. She was managed conservatively and advised not to use amphetamines again. She did not have any recurrence on 2-year follow-up.

Ischemic colitis is a relatively infrequent cause of acute lower gastrointestinal bleeding (6%–18% of cases) (1, 2). Among cases of ischemic colitis, a drug-induced etiology is an uncommon cause. Amphetamines, both prescription drugs and drugs of abuse, have been known to cause ischemic colitis (3, 4). Patients tend not to divulge their use of amphetamines. Identification of the root cause and avoidance of the use of the incriminating agents can be curative in such cases.

CASE DESCRIPTION

A 43-year-old woman with no previous significant medical illness except for hypothyroidism presented with sudden onset of lower abdominal pain and bloody diarrhea. Her hemoglobin level was 6.8 g/dL, and a blood transfusion was given. She denied prior gastrointestinal bleeding or known liver disease. A computed tomography scan of the abdomen was normal except for mesenteric fat stranding. She had no risk factors for atherosclerotic vascular disease. A workup for lupus and thrombophilia—including tests for antinuclear antibody, anti-DNA, protein C, protein S, anti-thrombin III, anti-phospholipid antibody, and prothrombin gene mutation—was negative. Mesenteric Doppler showed normal flow in the mesenteric vessels. A colonoscopy, performed 2 days after the presentation, showed mucosal bleeds, hemorrhagic nodules, inflammation, and other features in the sigmoid colon suggestive of ischemic colitis (Figure). Microscopic examination of the colonic mucosa also confirmed the diagnosis of acute mesenteric ischemia. At this point, she admitted using amphetamines. She had quit this habit but relapsed 2 days prior to admission and started snorting amphetamines again. A urine drug screen was positive for amphetamines. She was advised to avoid the use of amphetamines and did not have any events on follow-up.

DISCUSSION

Ischemic colitis, as the name suggests, develops from hypoperfusion of the colon. It might be the result of occlusive vascular disease or transient low-flow states, especially when the mesenteric vessels are diseased. Mesenteric vascular disease is a manifestation of atherosclerosis, and the risk factors are similar. The watershed areas of the colon such as the splenic flexure and rectosigmoid region are commonly affected with ischemic colitis. Ischemic colitis usually occurs in patients who are older than 60 years of age (5). The most common presenting symptom is abdominal pain. Other symptoms include abdominal distention, shock, sepsis, hematochezia, and diarrhea. Other causes of ischemic colitis include vasculitis, embolism, hypercoagulable states, colonic obstruction, and drugs (6). Ischemic
Colitis in younger patients should prompt the search for such causes. Exclusion of these causes is prudent before attributing ischemic colitis to drugs. Dietary supplementation with phentermine (an amphetamine-derived sympathomimetic) can be associated with ischemic colitis (3). Amphetamine-induced systemic effects are believed to be due to release of vasoactive amines. The central effects are caused by dopamine and the peripheral effects are due to norepinephrine. Intestinal ischemia may be due to splanchnic vasoconstriction but can also be due to necrotizing angitis (7, 8).

Colonoscopy and imaging modalities may be helpful in diagnosis. Mucosal bleeds, hemorrhagic nodules, edema, longitudinal ulcers, and gangrene may be observed on colonoscopy. However, none of these findings except for gangrene is specific for ischemic colitis (9). Thickening of the bowel wall may be observed with computed tomography and ultrasound.

Supportive management is generally advised in the absence of colonic perforation of gangrene. Bowel rest, intravenous fluids, antibiotics, and optimization of blood pressure and cardiac output are desirable. Avoidance of drugs that precipitated ischemic colitis is of paramount importance in drug-induced ischemic colitis. Early identification and management of complications, like gangrene of colon and peritonitis, is prudent.

About 1 in 5 patients with ischemic colitis require surgery due to such complications. Nonviable areas of bowel are resected during surgery. Patients with extensive areas of infarcted bowel have a high mortality rate.


Avocations

A cheetah and her cub in Tanzania. Photo copyright © Jed Rosenthal, MD. Dr. Rosenthal is a cardiologist in Dallas, Texas (e-mail: jedr2@sbcglobal.net).
Syphilitic proctitis is a rare disease that usually presents as proctitis, ulcer, and neoplasm but lacks pathognomonic clinical symptoms. It is thus difficult to diagnose and may be treated inappropriately. We report a 31-year-old man who had a hard, ulcerated mass that occupied the rectal and sigmoid colon wall and mimicked a tumor. Fortunately, a biopsy of the mass demonstrated *Treponema pallidum* organisms consistent with syphilitic proctitis. The patient was successfully treated with intravenous benzyl penicillin, resulting in improvement in his proctitis.

**CASE REPORT**

A 31-year-old man presented to the hospital with an 11-month history of rectal bleeding, tenesmus, a 20-pound weight loss, mucoid rectal discharge, and blurry vision. He had had receptive anal intercourse with multiple homosexual men. Rectal examination revealed a tender fungating mass protruding from the anal verge (Figure 1). The antibody for human immunodeficiency virus was positive, and the CD4 cell count was 240 cell/mL. Computed tomography (CT) of the abdomen and pelvis showed circumferential thickening of the rectum extending to the anal verge and multiple enlarged perirectal lymph nodes. Colonoscopy showed an irregular rectal mass segment and hyperemia and erosions involving the rectum and distal sigmoid colon.

The rectal mass was biopsied. Histological findings of the biopsy showed fragments of polypoid granulation tissue with prominent plasma cells on hematoxylin and eosin stain (Figure 2a) and abundant *Treponema pallidum* organisms on immunohistochemical staining consistent with syphilitic proctitis (Figure 2b). Rapid plasma reagin and Treponema antibody were positive. He underwent lumbar puncture and was confirmed to have neurosyphilis. The patient was treated...
for 3 weeks with intravenous benzyl penicillin, resulting in resolution of his visual complaints and improvement in the proctitis based on endoscopy. The endoscopy also revealed that the rectal mass had resolved (Figure 3).

DISCUSSION

There has been a reemergence of syphilis with a global increase in the incidence of sexually transmitted infections (1). Syphilitic proctitis is a rare complication, with most cases seen in patients who practice receptive anal intercourse. From 2005 to 2013, the Centers for Disease Control and Prevention estimated that the number of primary and secondary syphilis cases reported had almost doubled from 8,724 to 16,663 (2).

Syphilitic proctitis varies in presentation, including chancres in primary syphilis that spontaneously heal, mass-like lesions as seen in our patient, and ulcers (3). These features often overlap with inflammatory bowel disease, other infectious causes, and nonsteroidal antiinflammatory drug enteropathy. CT and colonoscopy findings typically show features overlapping with malignancies and nonspecific inflammatory changes. None of these findings confirm the diagnosis of syphilitic proctitis. Therefore, high clinical suspicion is imperative for expedient diagnosis. Tissue biopsy with staining for *T. pallidum* (though not always present) and infectious laboratory evaluations helped in reaching the correct diagnosis. First-line treatment is benzathine penicillin G.

![Figure 3. The fungating rectal mass resolved endoscopically after treatment with benzathine penicillin G.](image)

Pulmonary embolism following celiac plexus block and neurolysis

Scott A. McAninch, MD, Miles S. Raizada, MD, MBA, and Seth M. Kelly, MBA

Treatment of acute pain in chronic disease requires the physician to choose from an arsenal of pain management techniques tailored to the individual patient. Celiac plexus block and neurolysis are commonly employed for the management of chronic abdominal pain, especially in debilitating conditions such as cancer or chronic pancreatitis. The procedure is safe, well tolerated, and produces few complications. We present a case of pulmonary embolism following a celiac plexus block and neurolysis procedure. Further study is required to determine if celiac plexus ablation, alone or in combination with other risk factors, may contribute to increased risk for pulmonary embolism in patients seeking treatment for chronic upper abdominal pain conditions.

We present the first known reported case of pulmonary embolism following a celiac plexus block and neurolysis procedure in the outpatient pain clinic setting.

CASE PRESENTATION

A 23-year-old woman received a celiac plexus block with lidocaine and bupivacaine, followed by an ablation with 98% dehydrated alcohol diluted with Omnipaque 180 at the L1 level for pain related to chronic pancreatitis. The procedure was performed at an off-site pain management clinic. Within 20 minutes of beginning the procedure, the patient experienced a rapid onset of persistent, severe (10/10) right lateral chest pain with radiation to the center of her chest and below her right breast, epigastric tenderness to palpation, accompanied by dyspnea, palpitations, nausea, and vomiting.

She arrived at our emergency department (ED) within 30 minutes of symptom onset. Similar pain had not occurred in the past. Apart from her chronic abdominal pain, she denied any fever, chills, wheezing, hemoptysis, extremity swelling or pain, traumatic injury, diarrhea, constipation, or diaphoresis. The patient had driven 4 to 5 hours to the off-site pain clinic on the day of presentation. Although she had no recent surgeries, she indicated she had multiple hospitalizations, often for days to weeks at a time, for treatment of chronic pancreatitis. Medications included hydrocodone-acetaminophen (5/325 mg) and etonogestrel, which was implanted 3 weeks before the day of admission. She denied any tobacco, alcohol, or drug use.

No family members had venous thrombosis, blood clotting disorders, or vasculitis conditions.

Upon arrival at the ED, her blood pressure was 130/100 mm Hg; heart rate, 116 beats/minute; respirations, 18 breaths/minute; pulse oximetry, 98%; and temperature 99.7°F (37.6°C). She was mildly distressed, alert, oriented (×3), and cooperative. Physical exam disclosed only splinting with chest wall breathing movement. An abdominal exam revealed only mild, chronic, epigastric tenderness to palpation. Upper and lower extremities appeared normal with good pulses. The neurologic exam was normal. A 12-lead electrocardiogram in the ED demonstrated sinus tachycardia at a rate of 104 beats/minute, a S1QT3 pattern, and additional inverted T waves in V2 to V5 with normal ST segments and normal axis. A chest radiograph showed no acute findings. The lab results were significant only for carbon dioxide, 19 mmol/L; lipase, 107 U/L; and D-dimer, 1.05 μg/mL. A limited cardiac and pulmonary point-of-care ultrasound was normal. A computed tomography (CT) angiogram of the chest in the ED revealed nonocclusive pulmonary emboli, primarily within segmental branches of the left lower lobe and to a lesser extent the right lower lobe.

Treatment included aspirin, pain medication, and heparin bolus followed by continuous infusion. Upon admission, inpatient bedside sonography with color flow Doppler of the bilateral lower-extremity venous system showed no evidence of venous thrombosis. The patient was transitioned from heparin to apixaban for continued outpatient anticoagulation therapy. The anticardiolipin IgM level was 0.13 mg/dL (upper limit of normal 0.12), but IgG was normal. Factor V Leiden and prothrombin mutation markers were normal. The patient was discharged home with residual, but improved, mild pleuritic chest pain and occasional exertional dyspnea with instructions to follow up with her primary care physician. Two months after the ED visit, the patient had no recurrence of the chest pain or dyspnea or development of other thrombotic conditions.

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DISCUSSION

The celiac plexus block and neurolysis procedure is used for pain relief in selected painful upper abdominal conditions mediated by the celiac plexus, such as pancreatitis and upper abdominal cancer (1), and it may decrease the use of opioid pain medication in such conditions (2). The block and neurolysis procedures differ by their anticipated duration of pain control. The block provides temporary pain relief with injection of long-acting anesthetics or corticosteroids, whereas neurolysis provides permanent pain relief via destruction of the celiac plexus with either ethanol or phenol (3). The neurolytic block is achieved when either 50% to 100% ethanol or phenol is injected into or around the celiac plexus of nerves surrounding the aorta that carry pain information of the upper abdominal organs through sympathetic, parasympathetic, and visceral sensory fibers. Injection of ethanol may produce severe pain, so anesthetics, such as lidocaine or bupivacaine, are often injected around the celiac plexus beforehand or concurrent with alcohol to effectively provide a block. The injection procedure takes 10 to 30 minutes to complete and is often accompanied by procedural sedation. Imaging guidance for placement is by fluoroscopy, endoscopic ultrasound, CT scan, or magnetic resonance imaging.

The celiac plexus block and neurolysis procedure is generally well tolerated. Transient back pain and shoulder pain may occur due to local tissue and diaphragmatic irritation, respectively. Transient diarrhea (4) and orthostatic hypotension (5) may occur due to sympathetic nerve blockade. Significant complications related to celiac plexus block are uncommon. One recent study (6) demonstrated only four complications in 220 procedures. Paraplegia (7) as well as bowel and bladder dysfunction may result from inadvertent injection of anesthesia into a spinal artery. Pneumothorax, pericarditis, aortic dissection (8), and retroperitoneal abscesses have been reported in relation to the celiac plexus block. To date, we are unable to locate any reported cases of pulmonary embolism associated with the celiac plexus block.

Alcohol neurolysis is a well-established treatment in chronic pain management, often used in cases of intractable cancer-related pain that is refractory to other management therapies. We describe a 76-year-old woman with chronic toe neuritis who failed multiple treatments, including oral and topical analgesics, nerve blocks, and radiofrequency ablations. Alcohol neurolysis was performed via digit block of the toe resulting in 100% pain relief.

Alcohol neurolysis of digital nerves

Emily L. Walker, MD, Garrett K. Wright, MD, and Christopher J. Burnett, MD

Alcohol neurolysis is a well-established treatment in chronic pain management, often used in cases of intractable cancer-related pain that is refractory to other management therapies. We describe a 76-year-old woman with chronic toe neuritis who failed multiple treatments, including oral and topical analgesics, nerve blocks, and radiofrequency ablations. Alcohol neurolysis was performed via digit block of the toe resulting in 100% pain relief.

We describe a case of alcohol neurolysis via digital block of the toe which resulted in 100% pain relief for our patient.

CASE REPORT

A 76-year-old woman presented to our pain clinic with a primary complaint of sharp, stabbing pain affecting the distal interphalangeal joint of the right second toe. There was no history of trauma to the toe, and prior treatments included steroid injections by a podiatrist. She rated the pain a 9 out of 10 on a verbal rating scale. We elected to proceed with a radiofrequency ablation (RFA) of the superficial peroneal nerve at the level of the right second toe.

One month later, she presented for follow-up. She had achieved a 2-week period of 100% pain reduction, but the pain returned to baseline. The patient was utilizing antiinflammatory pain medication with minimal relief. We repeated the RFA and also started the patient on gabapentin 100 mg three times daily with a schedule for slow titration. Additionally, we ordered a compounded cream containing lidocaine 2%, prilocaine 2%, topiramate 2.5%, and meloxicam 0.09% as a topical adjunct.

Three months later, she returned after her second RFA and reported 100% pain relief for approximately 1 week. She did not tolerate the gabapentin well, reporting side effects of dizziness and somnolence. At that time, she requested that the podiatrist amputate her toe and her podiatrist agreed if pain management had exhausted all treatment modalities. After extensive discussion with the patient, we elected to perform alcohol neurolysis for her pain. Using aseptic technique, the right second toe was injected with 1.5 mL of 1% lidocaine forming a wheal around the base of the toe. Next, 1.5 mL of 98% dehydrated alcohol was injected in a similar fashion. The patient tolerated the procedure well and was discharged home with no apparent complications.

Three days postinjection, the patient experienced redness and swelling in her right second toe. She was seen in the emergency department where she was given intravenous clindamycin and discharged home with oral clindamycin. Significant laboratory findings at this time included an elevated erythrocyte sedimentation rate and C-reactive protein. She followed up in a podiatry clinic later that week where she was noted to have skin necrosis and cellulitis (Figure 1a) and was admitted to the hospital for intravenous antibiotics. Magnetic resonance imaging of the leg showed minimal soft tissue edema without evidence of an acute process, and an x-ray of the foot was normal. After 4 days in the hospital, she was discharged home with oral doxycycline and Norco.

Following discharge, she described the pain in her toe as 8 out of 10 on a verbal rating scale, but overall she was improving clinically (Figure 1b). She returned to the pain clinic for follow up 2 months from the date of the alcohol neurolysis. At that time, she was extremely satisfied with her pain control, reporting 0 out of 10 pain, and her cellulitis had completely resolved (Figure 1c).

DISCUSSION

Alcohol neurolysis is a technique to treat chronic pain, especially cancer pain (1). It is not commonly used for peripheral nerves; however, there have been reported cases of successful alcohol neurolysis for chronic pain conditions that affect peripheral nerves such as Morton’s neuroma, meralgia paresthetica, and poststroke spasticity.

Ultrasound-guided alcohol ablation has been described to treat Morton’s neuroma, and several studies have been performed describing the safety and efficacy of alcohol ablation.
in these cases (2–4). It has been described as a safe procedure that significantly reduces pain and may offer an alternative to surgery (2). One retrospective case series showed a reduction in mean pain score from 8.7 to 3.6, with the procedure proving safe in all patients (3).

Additionally, alcohol neurolysis of the lateral femoral cutaneous nerve (LFCN) has been described to treat meralgia paresthetica (5). While no large study has formally evaluated the use of alcohol neurolysis in this context, there have been isolated reports of alcohol neurolysis of the LFCN being a safe and effective method of treatment (5).

Two separate case series have also shown efficacy for alcohol neurolysis in treating poststroke spasticity. The first study showed alcohol neurolysis providing good relief of finger flexor spasticity in a cohort of 30 hemiplegic individuals (6). The second showed good relief of elbow flexion spasticity following alcohol neurolysis of the musculocutaneous nerve in a group of 20 hemiplegic patients (7).

To our knowledge, no study has investigated the use of alcohol neurolysis on digital nerves for chronic neuritis or tendinitis in humans, though there are reports of successful analgesia in horses following an alcohol ablation of palmar digital nerves (8).

For our patient, we sought a more permanent method of treating her debilitating pain from chronic digital neuritis. As a final interventional effort, we attempted alcohol neurolysis. Ultimately, she achieved complete pain relief but experienced an adverse event that was likely related to the procedure. Perhaps future injections should consist of a smaller volume of alcohol deeper into the tissue in an attempt to avoid the complication of necrosis and cellulitis.

Complex regional pain syndrome (CRPS) is a neurologic disorder that often results in debilitating chronic pain, but the diagnosis may elude providers as it is one of exclusion. A history of trauma may be elucidated. We report a case of CRPS and review the clinical findings, appropriate workup, and treatment options for the patient. The patient we describe went through an extensive workup before receiving the correct diagnosis. Delay in diagnosis leads to prolonged suffering for the patient and, at times, unnecessary invasive debridement procedures. Raising awareness of this entity may help physicians make the correct diagnosis early, as well as initiate a collaborative effort between neurology, anesthesiology, and dermatology to provide the patient the most favorable outcome.

We present a case of complex regional pain syndrome (CRPS) in a 41-year-old man to highlight the importance of early recognition and diagnosis to reduce the significant morbidity associated with this disease.

**CASE DESCRIPTION**

A 41-year-old white man presented to the emergency department with a severely painful, nonhealing ulceration on his left index finger after cutting his finger on bailing wire. He was evaluated in an emergency department and discharged. He returned several days later with increasing redness and pain, received a dose of intravenous vancomycin, and was discharged with oral trimethoprim/sulfamethoxazole. Several days later, the worsening pain was so severe that he requested amputation of his finger. Upon admission, his wound was debrided in the operating room. After several days of intravenous vancomycin, he was discharged with oral minocycline. All wound cultures performed over the course of his hospitalizations were negative for pathogens. Upon his fourth presentation, still in excruciating pain, the dermatology service was consulted for body tissue culture. Examination of his left index finger revealed a dry, heme-crusted ulceration with surrounding erythema and violaceous edema. He was otherwise healthy, but did suffer from depression and multiple suicide attempts in the past. He reported no drug allergies.

The biopsy for tissue culture was negative for fungus, bacteria, and acid-fast bacilli. A plain radiograph displayed soft tissue swelling. The diagnosis of CRPS following trauma was made.

**DISCUSSION**

CRPS is a condition that is aptly named, as it is often a complex entity to diagnose and manage. The disorder results from a neurologic dysfunction that produces severe and often debilitating pain. It most often affects extremities and may result from trauma or a vascular event. The condition has many pseudonyms, including reflex sympathetic dystrophy, algodystrophy, causalgia, Sudeck's atrophy, transient osteoporosis, and acute atrophy of bone, which adds to the confusion. In 1993, a consensus group settled on CRPS as an umbrella term.

The diagnosis of CRPS requires the presence of pain and sensory changes in a specific region following a noxious event. The pain is out of proportion to the inciting stimulus and can be associated with erythema, swelling, temperature changes,
and abnormal pseudomotor activity (1). There are two types: type I has no apparent nerve injury (90%) and type II has an identifiable nerve injury.

The reported skin changes are nonspecific and require awareness of this entity for it to be included in the differential diagnosis. Sundaram et al reported that the most common skin-related changes include edema (58%), erythema (54%), dermatitis (35%), erythematous papules (23%), atrophy (23%), ulceration (13%), and bullae (13%) (2). Our patient presented with edema, erythema, and a nonhealing ulceration in addition to severe pain. Other disorders often considered first in the differential are infection, peripheral vascular disease, peripheral neuropathy, deep venous thrombosis, scleroderma, thoracic outlet syndrome, rheumatoid arthritis, and perhaps even a conversion or factitious disorder. Infection was initially considered the likely diagnosis for our patient, resulting in a debridement procedure.

There are three stages of CRPS. In stage 1, patients may feel burning pain and develop cutaneous signs of edema, erythema, or dermatitis but lack underlying bony involvement. During stage 2, there can be worsening edema of the soft tissues, skin thickening, and muscle wasting. In stage 3, or chronic CRPS, there is decreased range of motion, contractures, atrophy of the skin, and significant demineralization of the bone. However, one study found no evidence of three consecutive phases of the disease (3). Patients diagnosed in stage 3 portend a worse prognosis and should be treated aggressively. Early manifestations are often more consistent with an inflammatory reaction than a disturbance of the nervous system, which may lead to a delay in diagnosis (3).

CRPS is a clinical diagnosis of exclusion, but studies that may aid in making the diagnosis early in the disease are automatic function testing, bone scintigraphy, plain radiographs, and magnetic resonance imaging (MRI). One study found bone scans superior to plain radiographs and MRI for ruling out CRPS (4).

Treatment should be instituted immediately upon diagnosis to alleviate the debilitating pain patients suffer with this disorder. Conservative measures include nonsteroidal antiinflammatory drugs, tricyclic antidepressants, gabapentin, topical capsaicin, bisphosphonates, and low-dose oral glucocorticoids (5–8). More aggressive therapies for refractory cases include nerve and spinal cord stimulation, regional nerve blocks, and sympathectomy (9). Smoking cessation can result in improvement (10). No matter the stage, physical and occupational therapy should be initiated upon diagnosis (11). We hope to close this practice gap and bring more awareness to this painful condition.

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Bevacizumab-induced pityriasis rubra pilaris-like eruption

Shannon Brown, MD, J. Wesley Fletcher, MD, and Katherine H. Fiala, MD

Pityriasis rubra pilaris is a rare inflammatory disorder characterized by follicular papules on an erythematous base often exhibiting islands of unaffected skin, follicular plugging, and palmoplantar hyperkeratosis. While vitamin A deficiency and autoimmune reactions have been hypothesized as possible etiologies of this condition, pityriasis rubra pilaris-like eruptions secondary to medications are extremely rare. To our knowledge, only three other cases have been reported, and pityriasis rubra pilaris has never been reported in association with bevacizumab. We present a 70-year-old man who developed erythroderma both clinically and histologically consistent with pityriasis rubra pilaris 10 days after intravitreal injection of bevacizumab for age-related macular degeneration. As immune-modulating drugs grow in their application for a host of diseases, recognition of associated medication complications is important.

Table 1. Causes of erythroderma

<table>
<thead>
<tr>
<th>Cause</th>
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<tbody>
<tr>
<td>Psoriasis</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
</tr>
<tr>
<td>Drug reactions</td>
</tr>
<tr>
<td>Cutaneous T-cell lymphoma</td>
</tr>
<tr>
<td>Pityriasis rubra pilaris</td>
</tr>
<tr>
<td>Pemphigus</td>
</tr>
<tr>
<td>Ichthyoses</td>
</tr>
<tr>
<td>Staphylococcal scalded skin syndrome</td>
</tr>
<tr>
<td>Toxic epidermal necrolysis</td>
</tr>
<tr>
<td>Norwegian scabies</td>
</tr>
<tr>
<td>Idiopathic</td>
</tr>
</tbody>
</table>

CASE REPORT

A 70-year-old Caucasian man presented to the dermatology clinic with a 10-day history of exfoliative dermatitis. It began as a burning sensation on the scalp and quickly progressed to diffuse erythema and edema with intense pruritus. He had received prednisone in the emergency department 4 days prior to his clinic visit, which significantly improved his symptoms. Two weeks before presenting to the dermatology clinic, the patient received an intravitreal injection of bevacizumab for a new diagnosis of age-related macular degeneration. He denied a history of known drug allergies or previous adverse dermatologic reactions to medications. Of note, he did have a history of malignant melanoma that was excised from the right forearm in 2008, with no signs of recurrence. His past medical history was significant for hypertension and hypercholesterolemia, for which he took valsartan and simvastatin.

On initial exam, he had an erythematous, scaly, exfoliative erythroderma with “islands of sparing” affecting the face, scalp, trunk, hands, and feet (Figure 1). He was continued on...
a prednisone taper and prescribed desonide 0.05% cream for the face and triamcinolone 0.1% topical cream for the body. Basic laboratory results were normal. He returned to the clinic 1 week later complaining of worsening symptoms when the prednisone dose was tapered. At that time, he had significant erythema and scaling of the scalp and face, extending onto the neck. Additionally, his palms and soles had large patches of erythema and significant scaling (Figure 2). A 4 mm punch biopsy from the right postauricular neck was performed showing foci of parakeratosis and follicular plugging consistent with PRP. The biopsy also showed a superficial perivascular infiltrate of lymphocytes with eosinophils, more consistent with a drug-induced eruption. Given his recent initiation of bevacizumab, clinical presentation, and histopathological findings, the diagnosis was considered to be a PRP-like eruption secondary to bevacizumab. He was switched to a higher prednisone taper and prescribed clobetasol 0.05% ointment. He showed great improvement with this combination of systemic and topical corticosteroids within 2 weeks.

DISCUSSION

Cutaneous adverse reactions to bevacizumab are not uncommon; however, this is the first reported case of a PRP-like reaction induced by an intravitreal injection of bevacizumab. Since the pathogenesis of primary PRP is unclear, we were unable to completely rule out other possible causes such as solid organ malignancy and infection. Nonetheless, our patient’s rapid clinical improvement with topical and systemic steroids, along with the presence of eosinophils on histopathology, suggests a drug-induced reaction over primary PRP.

Three similar cases of PRP-like drug reactions have recently been reported. The first was induced by sorafenib, a multitargeted kinase inhibitor (2). Sorafenib, like bevacizumab, is known to inhibit angiogenesis through vascular endothelial growth factor. It is possible that by inhibiting this signaling pathway, downstream effects of cell proliferation are altered, leading to a unique cutaneous reaction. PRP-like reactions have also been reported with telaprevir, a protease inhibitor, and imatinib, a kinase inhibitor (3, 4). Similar to our case, these reported cases of PRP-like drug eruptions resolved quickly with treatment, in contrast to primary PRP, which is usually persistent. Physicians should be aware that PRP-like drug reactions are occurring more frequently and may be associated with intravitreal injections of bevacizumab.

The intellect of man is forced to choose  
Perfection of the life or of the work.  
—William Butler Yeats, “The Choice”

William Osler (1849–1919), the English-speaking world’s best-known and best-loved physician at the turn of the 20th century, continues to inspire through his personal example and his writings, but what was he really like? We have no videotapes of Osler in action, no recordings of his voice, and must therefore rely on what contemporaries said supplemented by such evidence as portraits done from life. Critics consider the 1908–1909 portrait by Seymour Thomas (1868–1956) (Figure 1) the best by far of six oil-on-canvas portraits of Osler done from life, including those by the more-acclaimed US portraitists John Singer Sargent and William Merritt Chase (1–3). Osler called it “the best pictorial diagnosis I have ever seen” and told Thomas “I am at your service.” A reappraisal of Seymour Thomas explains why his portrait makes us feel much as the artist did in Osler’s presence, which is the original English-language definition of “empathy.” Thomas told his subject that “I feel that you can look clear through me and see the wall on the other side.” The intensity of Osler’s gaze affects us similarly. The portrait satisfied Osler, but his wife, Grace Revere Osler, never warmed to it, perhaps because it depicts so clearly a highly focused, agenda-driven man. Helen Thomas used the portrait to promote her husband’s business, and, after a tortuous history, the portrait eventually returned to Oxford University, where it now hangs inconspicuously in the Radcliffe Science Library.

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SEYMOUR THOMAS

Stephen Seymour Thomas, a prodigy, was born in San Augustine, Texas, and raised in Dallas and then San Antonio. At age 8, he did a pencil drawing that won an award at the North Texas Fair Association, and he became known as the “Boy Artist of Texas” (4). At age 12 he illustrated a book, and by age 15 he
could complete sophisticated oil-on-canvas compositions. At age 17 he began spending months at the Art Students League in New York, where his teachers included William Merritt Chase, and at age 20 he went to Paris to study at L’Académie Julian and at L’École Des Beaux Arts. In 1891, at age 23, he submitted four works to the Paris Salon, all of which were accepted. Soon thereafter he met a fellow American art student, Helen Montmorency Haskell of San Francisco, a tall, slender redhead 8 years his senior, and fell hopelessly in love.

The year 1892 became the *annus mirabilis* for Thomas, as it did for his future subject William Osler and for the same reasons: completion of a career-defining masterpiece and marriage to a woman who then promoted his career. Osler’s 1892 masterpiece was *The Principles and Practice of Medicine*, which became the English-language standard, and his marriage to Grace Revere Gross that year enabled him to establish a household where he conducted a successful practice. Thomas’s 1892 masterpiece was *Victim Innocente*, a large canvas depicting a Sister of Charity mortally wounded on a battlefield while attending a soldier. Its huge success at the Paris Salon, wrote Thomas’s biographer, “tilted the scales in his favor” (4) in his courtship of Helen Haskell and enabled him, at 24, to become the youngest person at that time to be listed in *Who's Who in American Art*. He went on to exhibit at the Paris Salon 20 consecutive years, to receive Gold Medals there in 1901 and 1904, and to reap such additional honors as the French Chevalier de la Légion D’Honneur (1905). Although Thomas excelled at landscapes and genre scenes in the style of the later French Impressionists and could do massive historical paintings such as his *General Sam Houston at the Battle of San Jacinto* (1892), he increasingly concentrated on portraits to afford Helen the lifestyle he felt she deserved. She in turn sublimated her artistic career for her husband’s and never looked back. By December 1908, when William Osler while on sabbatical in Paris rapped on the studio door at No. 11 Impasse Ronsin, Thomas was a sought-after portraitist.

Hugh Hampton Young, Thomas’s friend from high school and Osler’s from Johns Hopkins, orchestrated the meeting (5). As Thomas described the encounter 40 years later to Los Angeles neuropathologist Cyril B. Courville, the visitor stated: “I am Doctor Osler, and I have a letter of introduction from our mutual friend, Dr. Hugh Young.” Thomas replied: “Oh, yes, Doctor Young told me to be on the lookout for you.” Osler, projecting his own opinion onto their mutual friend, told Thomas: “You see, Doctor Young doesn’t think so much of the portraits which have been painted of me thus far and is of the opinion that you can do a better one.” Thomas replied, “I shall be pleased to try” (1).

**THE ARTIST AND HIS SUBJECT**

The term “empathy,” now a core competency in medicine, entered the English language in the context of aesthetic experience as a 1909 translation from the German *Einfühlung* (“in-feeling”), coined in 1873 by the philosopher Robert Vischer to denote the human capacity to enter into a work of art or literature and experience emotions similar to the artist’s (6, 7). It would be difficult to imagine a more clear-cut illustration of “empathy” in the original sense than Seymour Thomas’s portrait of Osler. Thomas told his subject: “I feel that you can look clear through me and see the wall on the other side” (1). The portrait affects us much the same way. Osler’s eyes in the portrait, wrote the pathologist Maude Abbott, make us feel “the quiet fire of their expression” (8). Osler’s biographer Michael Bliss observed that whereas most portraits of Osler “feature a stiff, wooden figure,” the “difference in the Thomas portrait is his eyes, which are particularly shadowed, dark, and intense” (9). By contrast, Osler’s eyes in the portraits by Sargent and Chase suggest little or nothing about the subject’s personality. Let’s examine why this is the case.

Cecilia Steinfeldt wrote in her biography of Thomas: “When compared to the work of his peers,” Thomas’s work lacks “the flamboyance of Sargent, the vitality of Chase, and the romantic ambience of [James Abbott McNeill] Whistler.” She then stated that Thomas had “a flair for capturing the personality of his subjects,” and therefore his work “provides an insight to people and places not apparent in the work of other painters” (4). Whistler did not paint Osler; Chase’s portrait has been described as “beign and pleasing” (1); and the same might be said of previous portraits of Osler by Henry Scott Tuke (1885), Robert Harris (1903), and Thomas C. Corner (1905). The key comparison, then, is between Sargent and Thomas (Figures 2 and 3).

To confirm that Thomas’s work lacks “the flamboyance of Sargent,” we need look no further than two paintings of men in academic regalia: Sargent’s *The Four Doctors* (1905) and Thomas’s *The Big Three* (1929) (Figure 3). Sargent grouped his subjects, declared “this isn’t a picture,” and insisted on bringing in a large Venetian globe, which required dismantling a door frame. He situated the men around the globe, put his copy of Petrarch on the table, and painted a replica of El Greco’s *St. Martin and the Beggar* (c. 1597–1599) in the background. *The Four Doctors* met instant acclaim and today leaves a lasting

![Figure 2. Details of portraits of William Osler by (a) John Singer Sargent (from *The Four Doctors*, 1905), and (b) S. Seymour Thomas (sketch made in 1944 for Dr. Esther Rosencrantz from the 1908–1909 portrait). Courtesy of the Alan Mason Chesney Medical Archives of the Johns Hopkins Medical Institutions (painting by Sargent) and the Archives and Special Collections, Library and Center for Knowledge Management, University of California, San Francisco (sketch of Osler by Thomas).](image-url)
portraitists had found his expression dour and had commented on his complexion, which Osler attributed to being descended from the “Black Celts of Cornwall” (1). (The Cornish have been called “decidedly the darkest people in England” [11], possibly because of a high density of genes originating from Spanish fishermen—Celtiberians—who crossed the Bay of Biscay between 4000 and 5000 BC.) Only after close observation of Osler’s personality did Thomas begin to paint.

He painted quickly. The finished portrait took only about 11 hours, divided into eight or nine sittings, usually in the late morning or at noon. The Osler’s son, Revere, in Paris for the Christmas season, sometimes came and sat quietly on a couch while the artist worked. On one occasion Osler brought a bevy of Canadian girls (the daughters of friends who were visiting Paris) who chattered the entire time. Thomas worked while the paint was still wet and later said that he did not retouch a single spot, add a single highlight, or correct a single detail. It was a classic example of premier coup (also known as alla prima or direct painting: applying each stroke of the brush with the intent that it be part of the final statement, with no retouching or overpainting after the first layer of paint has dried). Thomas considered it the easiest portrait he’d ever done. He told Osler: “You have painted your own portrait!” (1).

At least seven statements—five from Osler and two from Thomas—attest to Osler’s satisfaction. After the preliminary sketch Osler beamed: “This is the best pictorial diagnosis of me I have ever seen” (1). While the work was in progress he wrote a friend that “Seymour Thomas, an American artist, is doing [a portrait of me] . . . very good so far” (10). He wrote another friend when the painting was completed, “By the way, T’s picture of me is A-1. Really, I think, a first class job” (5). He wrote a third friend that Thomas had really “got him” (12). To these and other friends he sent copies of a photograph taken of the painting, inscribed “This is my portrait. W.O.” (1). Thomas-as-for his part wrote a journal editor: “I consider the portrait one of my best works. It has the most enthusiastic approval of Dr. O. & [he] says that it is the only one of the many that have been painted of him that he considers an unqualified success” (13). And years later Thomas told his neighbor the urologist William Goodwin that it was “rare to have both painter and subject so pleased with the results. He [Osler] said after it was completed, ‘This is my real portrait’” (5).

What, then, does the “real portrait” say about Osler in addition to the intensity of his gaze? On the one hand, and as many said about Osler during his lifetime, it suggests a focused, well-organized, agenda-driven man, a man who seemingly made the most of every waking minute, a man who would have risen to the top of just about any profession he chose (14). On the other
hand, the dark circles around his eyes connote chronic stress. The late Meyer Friedman attributed periorbital hyperpigmentation to chronic excess of melanocyte-stimulating hormone (secreted by the anterior pituitary along with adrenocorticotropic hormone in response to stress) and averred that “its presence in Caucasians invariably indicates severe Type A behavior” (15). Although the etiology of periorbital hyperpigmentation is multifactorial and in Osler’s case might reflect Celtiberian ancestry, its strong association with stress (71% of 200 patients) was found in a recent study from India (16). Osler’s countenance in the Thomas portrait contrasts strikingly, for instance, with the sunny countenance of Nobel Laureate Robert A. Millikan in Thomas’s preliminary sketch for The Big Three (Figure 4).

We should point out that, although photographs and portraits of Osler in his later life nearly always project solemnity, he was in person exceptionally friendly and often playful. One contemporary remarked on Osler’s “dark penetrating eyes which seemed to see more than to look and which in moments of humour mirrored merriment” (17). Still, there lingers a debate as to whether an essential melancholy lurked beneath Osler’s outwardly cheerful disposition. We might add that Thomas—whose portraits are devoid of the cynicism sometimes found in Sargent’s work—considered Osler “a truly great human being with a gift of universal understanding” (1).

EPILOGUE

Osler never sat for another oil-on-canvas portrait. But despite his satisfaction with the Thomas portrait, and even though Hugh Young had paid for it in advance, the Oslers neither kept the portrait nor suggested where it should hang. Thomas exhibited it at the 1909 Paris Salon, where many called it the year’s best portrait even though Thomas was by then hors concours—ineligible for a medal because he’d already received the maximum number. In 1914 Thomas returned to the United States, taking the Osler portrait with him (Figure 5). One story goes that Osler flippantly remarked to Thomas, “As long as you keep this portrait, you will have a good doctor with you” (1, 3, 5). The more plausible explanation constitutes a tale of two wives: Grace Osler never warmed to the portrait (1, 3), but Helen Thomas loved it and subsequently used it as the centerpiece for tea parties during which she recruited clients for her husband’s business.

To the extent that a husband’s near-constant companionship determines a wife’s marital satisfaction, Helen Thomas had it much better than Grace Osler. Osler was the quintessential public man. Even when at home in Oxford, he would invite large numbers of people to 13 Norham Gardens (the “Open Arms”) and expect Grace to entertain the guests whenever he retreated to his study. A photograph of the Oslers in their backyard shows him preoccupied with his reading while his wife and their son enjoy the moment (Figure 6). Seymour Thomas, by contrast, was nearly always at home in his studio or doing something with Helen. After she died in 1942, Thomas wrote: “In all our fifty years together we never separated for twenty-four hours and we scarcely had a thought that we didn’t share” (4). Although the Oslers’ marriage was by all accounts a satisfactory one, no surviving photograph shows a couple entranced with each other, as does a photograph of Helen and Seymour Thomas in the yard of their California home appropriately named “Cuddle Doone” (Figure 6).
Among the Osler devotees who dropped by Thomas's studio in La Crescenta, California, through the years were three whose interviews with Thomas provide much of what we know about the Osler portrait: Maude Abbott, Cyril Courville, and Willard Goodwin (1, 5, 8). In 1949 Courville and British neuropathologist William Henry McMenemey hinted to Thomas that the painting ultimately belonged at Oxford or elsewhere in Great Britain. Two authorities at Christ Church College, Oxford, wrote Thomas that if donated the portrait would hang in the Hall where it would be the first by an American artist "to adorn these walls" (18, 19). Thomas sent the portrait to Christ Church College—which then chose not to display it! It now hangs inconspicuously in the reading room on the seventh floor of the Jackson Wing of the Radcliffe Science Library at Oxford, unlabeled and facing away from the entrance. In all likelihood, students, if they notice it at all, are blissfully unaware of its status as the best portrait to life of a man who in his day was the English-speaking world's most celebrated physician. Perhaps Grace Osler ultimately had her way.

Acknowledgments

I thank archivists at McGill University, the University of Pennsylvania, the Johns Hopkins University, the California Institute of Technology, the University of California at San Francisco, Christ Church College, Oxford University, and the Witte Museum, San Antonio, Texas. I thank John M. Bryan for comments on the manuscript.

13. Seymour Thomas to the Editor of ______ [not stated], copy of undated letter. Texas Artist Collection, Box #18, Seymour Thomas Paintings, Osler. Witte Museum Archives, Witte Museum, San Antonio, Texas.
Baylor College of Medicine, Baylor Scott & White Health announce collaboration on biomedical research

Baylor College of Medicine and Baylor Scott & White Health have entered into an agreement to expand biomedical research in North and Central Texas. “With this joint operating agreement, we bring together the strengths of both institutions, which no doubt will result in more research of the highest quality,” said Dr. Paul Klotman, president and CEO of Baylor College of Medicine. “The clear winners are the residents of Texas, who will see an acceleration of efforts to provide new therapies.”

“This collaboration is exciting for many reasons, the most important of which is the positive impact we expect it will have on patient care as we’re able to translate findings from the laboratory to the bedside,” said Joel T. Allison, president and CEO of Baylor Scott & White Health. “It’s also gratifying to see two strong Baylor brands coming together to advance biomedical research.”

Baylor College of Medicine has the most funding from the National Institutes of Health (NIH) of any medical school in Texas. In 2015, the college received $227.8 million in NIH funding and $348.9 million in total funding for sponsored projects.

Baylor Scott & White Research Institute (BSWRI) collaborates with the medical industry to develop its technology and intellectual property to bring novel treatments to its patients. BSWRI has a more than $100 million operating budget, conducting 2000 research studies in more than 60 medical specialties in 250,000 square feet of research space.

“We’re proud of the research we’ve done to provide advanced treatment options to our patients and are thrilled to take those efforts to the next level by collaborating with one of the largest, most respected biomedical research programs in the United States,” said Dr. Michael A. E. Ramsay, president of BSWRI. “This collaboration raises our profile in the research community and will ultimately mean we’re able to positively impact even more lives.”

A search committee is now being established to recruit a chief scientific officer, who will oversee the collaborative effort and serve as a section chief in the Baylor College of Medicine Department of Medicine. The leader will report to Dr. Adam Kuspa, Baylor College of Medicine senior vice president, dean of research, and dean of the Graduate School of Biomedical Sciences, and will work closely with BSWRI. The collaboration will be governed by a Research Oversight Council, composed of eight members, equally representing both institutions.

New faculty will be hired in both Dallas and Temple as Baylor College of Medicine faculty, and current faculty will transition to Baylor faculty appointments over time. “We expect by growing the number of research faculty and staff, and incorporating Baylor College of Medicine’s research model, we will be able to substantially increase the level of scientific innovation and the number of new therapies available to patients,” said Dr. Kuspa. “This model also will provide educational opportunities in the future.”

Landmark study may pave the way for personalized treatment of lupus and other complex autoimmune diseases

New research that may dramatically improve drug development for systemic lupus erythematosus patients was published April 21, 2016, in Cell. The paper, “Personalized immunomonitoring uncovers molecular networks that stratify lupus patients,” was written by Dr. Virginia Pascual, principal investigator of the study and researcher at Baylor Institute for Immunology Research, part of BSWRI.

Lupus is a complicated condition that’s difficult to diagnose—no single test can definitively detect it—and complex to treat since no two cases are alike. Clinical trials for effective drug treatments have had limited success. In this study, Dr. Pascual and her team aimed to understand the molecular diversity of the disease in an effort to make future drug development easier and more effective. “The results included in this paper provide an explanation for why clinical trials fail in lupus and open the door for true personalized approaches to drug discovery and treatment in this disease,” Dr. Pascual said.

Researchers studied the transcription of genes in 924 blood samples from 158 pediatric lupus patients from Texas Scottish Rite Hospital for Children clinics and other children’s hospitals for up to 4 years. This personalized immunomonitoring approach, which measures gene expression activity of different cell types, allowed researchers to classify patients into seven groups with similar molecular disease structure at the time of both disease flares and remissions.

Dr. Marilynn Punaro, medical director of rheumatology at Scottish Rite Hospital, and members of her team are coauthors of the study, which may improve clinical trial design and implementation of tailored therapies in lupus and other genetically and clinically complex autoimmune diseases. “This is a landmark study that has the potential to dramatically improve treatment and quality of life for the hundreds of thousands of people suffering with lupus,” Dr. Pascual said.

Researchers find new ways to manipulate cells linked to chronic respiratory disease

A new study conducted at Baylor University Medical Center at Dallas examined the regulation of certain immune cells and revealed how they can be manipulated to reduce severity of symptoms in inflammatory diseases such as asthma. The paper, titled “IL-1 is a critical regulator of group 2 innate lymphoid cell function and plasticity,” was published in Nature Immunology.

Recently a new class of immune cells found in the lungs—group 2 innate lymphoid cells (ILC2 cells)—has been studied for their role in triggering asthma symptoms such as mucus production and hypersensitive airways. In this study, researchers uncovered that a certain cell-secreted molecule, interleukin-1 (IL-1), interacts with ILC2 cells and causes them to multiply. Manipulation of interactions between ILC2 cells and IL-1 cytokine may lead to better treatment for asthma patients.

“We’re really proud of this work because it could point to potential therapies for treating chronic inflammatory diseases such as asthma,” said LuAnn Thompson-Snipes, PhD, adjunct professor and assistant investigator at the Baylor Institute for Immunology Research, an arm of BSWRI. “As we learn more about the regulation of our cellular immune responses, we come closer to paving the way for a cure.”

CEO Joel T. Allison announces intent to transition to advisory role in early 2017

Joel T. Allison, FACHE, and the Baylor Scott & White Holdings Board of Trustees have announced plans for Allison to transition from his
current role as president and CEO of Baylor Scott & White Health to senior advisor to the chairman of the board. The transition is set for February 1, 2017, Allison’s 69th birthday. In his new role, Allison will advise the board chairman in the areas of advocacy, philanthropy, and medical education.

“I’ve been blessed—I was called into this career that I love. So while I’ve spent the past 40-plus years working in health care, I feel I haven’t worked a day in my life,” said Allison. “Now, I’m looking forward to the next phase—one in which I’ll still remain engaged in an advisory role to the chairman, while enjoying more time with my wife and six grandchildren.”

(Continued on page 345.)

UPCOMING CME PROGRAMS

The A. Webb Roberts Center for Continuing Education of Baylor Scott & White Health is offering the following programs:

- **Complex Care: Treatment Trends and Improved Outcomes**, August 13, 2016, Santa Fe, New Mexico
- **Complex Care: Treatment Trends and Improved Outcomes**, September 17, 2016, Greenville, Texas
- **Chest Cancer 2016**, October 28, 2016, Baylor Charles A. Sammons Cancer Center, Dallas, Texas

For more information, call 214.820.2317 or visit www.cmebaylor.org.

RECENT GRANTS

- **Pharmacometric optimization of second-line drugs for multidrug-resistant tuberculosis treatment**
  Principal investigator: Tawanda Gumbo, MD
  Sponsor: University of Cape Town/National Institutes of Health
  Funding: $27,757
  Award period: 2/15/2016–1/31/2017

- **Project WOWii: developing and testing a web-based intervention to promote exercise among those with spinal cord injury**
  Principal investigator: Katherine Froehlich-Grobe, PhD
  Sponsor: National Institutes of Health
  Funding: $193,818
  Award period: 1/17/2016–9/30/2016

- **Glycemia reduction approaches in diabetes: a comparative effectiveness study**
  Principal investigator: Priscilla Hollander, MD, PhD
  Sponsor: George Washington University/National Institutes of Health
  Funding: $237,173
  Award period: 8/1/2015–7/31/2016

- **Families Improving Together (FIT) for weight loss**
  Principal investigator: Heather Kitzman-Ulrich, PhD
  Sponsor: University of South Carolina/National Institutes of Health
  Funding: $17,755
  Award period: 1/1/2016–6/30/2016

- **Texas Center for Minority Health Education, Research, and Outreach**
  Principal investigator: Heather Kitzman-Ulrich, PhD
  Sponsor: University of North Texas Health Science Center/National Institutes of Health
  Funding: $6,249
  Award period: 1/1/2016–5/31/2016

- **Baylor Core Clinical Center for the Cardiothoracic Surgical Network**
  Principal investigator: Michael Mack, MD
  Sponsor: National Institutes of Health
  Funding: $388,129
  Award period: 2/1/2016–1/31/2017

- **DC-ASGPR as a novel target for controlling graft-versus-host disease and allograft rejection**
  Principal investigator: SangKoon Oh, PhD
  Sponsor: National Institutes of Health
  Funding: $392,000
  Award period: 4/1/2016–3/31/2017

- **Operational tolerance biomarkers of immune senescence and lymphocyte exhaustion following adult liver transplantation**
  Principal investigator: Goran Klintmalm, MD, PhD
  Sponsor: Benaroya Research Institute/National Institutes of Health
  Funding: $89,144
  Award period: 2/1/2016–1/31/2017

- **Mitophagy and Paneth cell defects in intestinal inflammation**
  Principal investigator: Arianne Theiss, PhD
  Sponsor: Broad Medical Research Program at the Crohn’s & Colitis Foundation of America
  Funding: $109,643
  Award period: 4/1/2016–3/31/2017

- **Methylation biomarker development for noninvasive detection of colorectal cancer**
  Principal investigator: Ajay Goel, PhD
  Sponsor: National Institutes of Health
  Funding: $315,983
  Award period: 5/1/2016–4/30/2017

- **Quantifying infectiousness of undiagnosed tuberculosis cases and impact of enhanced community**
  Principal investigator: Tawanda Gumbo, MD
  Sponsor: Civilian Research and Development Foundation/National Science Foundation
  Funding: $178,866
  Award period: 4/22/2016–9/30/2016

- **Novel innate and adaptive immunity pathways lead to human systemic autoimmunity**
  Principal investigator: Virginia Pascual, MD
  Sponsor: National Institutes of Health
  Funding: $183,081
  Award period: 5/1/2016–4/30/2017
PHILANTHROPY NOTES

Campaign 2015: Baylor Makes Us All Better surpasses $250 million goal

On April 26, 2016, Baylor Health Care System Foundation held “A Night of Gratitude” at the Dallas Country Club to celebrate its recently completed initiative, “Campaign 2015: Baylor Makes Us All Better.” More than 300 donors, board members, and Baylor Scott & White Health executive leadership from throughout the community attended to mark the successful completion of the first comprehensive fundraising campaign in the Foundation’s history. This unprecedented campaign exceeded the original $250 million goal to invest in patient-focused programs, innovative research, medical education, capital, and advanced technology for Baylor Scott & White Health—North Texas.

Campaign 2015 received wide support from the Dallas philanthropic community. To date, nearly 90,000 gifts from more than 30,000 donors helped to raise almost $275 million for Campaign 2015, including 40 gifts of $1 million or more. These investments to Campaign 2015 have already begun to move mountains; we now have an advanced center for the treatment of cancer; our solid organ transplant center has been elevated to a new level of excellence; we have introduced an innovative comprehensive model of care for those suffering with Alzheimer’s; we are working on a project to provide free lodging for cancer patients and their caregivers who travel to Dallas for treatment; and we have supported a program to greatly improve care for our geriatric patients.

“We are grateful for the outpouring of support from generous philanthropists, foundations, corporations, and leaders in the community. Our donors know their investment is making a significant difference in our community’s health. They are part of something historic and meaningful,” said Rowland K. Robinson, president of Baylor Health Care System Foundation. “As we look forward, we remain dedicated to our mission to heal, to offer hope, and to improve lives. We can—and will—continue to move mountains.”

Steen, Horner families support home-away-from-home for cancer patients

The American Cancer Society selected Baylor University Medical Center at Dallas as the location of its newest Hope Lodge, a home-like facility that offers free accommodations for cancer patients who have to travel long distances for their care. Baylor Health Care System Foundation is grateful for two recent gifts that will help bring the vision of Hope Lodge Dallas to reality. These two gifts—$5 million from the Don and Trudy Steen Charitable Foundation and $1.25 million from the Horner Family—are instrumental to Hope Lodge Dallas, which will be 100% supported by philanthropy.

For both of the families, the gifts are personal and representative of a long history of giving to Baylor. Don Steen, who died of a form of leukemia in 2014, was a long-time supporter of the Baylor Foundation. During his illness, he and his wife, Trudy, noticed many cancer patients who struggled with taking care of their families while commuting long distances to receive medical care. When Trudy learned of the plans for Hope Lodge Dallas, she decided that contributing to it would be a way to honor Don, who founded United Surgical Partners International Inc. (USPI), a short-stay surgical facility company. “I think Hope Lodge will be a wonderful space where cancer patients can feel comfortable and concentrate on getting better,” Trudy said.

Several of Don’s friends are supporting the effort through the Friends of Don Steen Campaign. Among them are Bill Wilcox, CEO of USPI, and Ken Newman, a close personal friend of Don’s. “We were both deeply touched and honored to be asked by Trudy to make remarks at Don’s memorial service,” they stated in a letter that was sent to friends of the Steen family. “We’re both now honored to support this project in his memory.”

Thanks to the generous gift from the Horner Family, Hope Lodge Dallas will include a healing garden to support patients’ spiritual and emotional healing. What’s unique about the Horner Family Garden of Hope is that it will also feature a butterfly garden within, designed with plantings such as milkweed, marigold, and lantana, which are proven to draw and feed butterflies. A plaque honoring the jewelers of the family’s jewelry company, Premier Designs, will be featured in the butterfly garden.

The Horner Family have been loyal supporters of Baylor, and their gifts have provided significant support for Baylor’s fight against cancer and have also led to the Joan Horner Interfaith Prayer Garden at Baylor Dallas and to the naming of The Horner Family Chapel in the Baylor Charles A. Sammons Cancer Center. As patients and their families visit the healing garden at Hope Lodge, the Horner family’s desire is that they will find peace and hope that will give them comfort during their healing process.

Ginny Sillers learns a better way to give an IRA

In 2007, Ginny and Don Sillers set up a significant estate gift for Baylor Health Care System by naming Baylor Health Care System Foundation a beneficiary of Don’s individual retirement account (IRA). This estate gift was in thanks for Ginny’s physicians and other caregivers who saved her life in 1989 when she received a liver transplant at Baylor Annette C. and Harold C. Simmons Transplant Institute at Baylor University Medical Center at Dallas. According to their plan, upon their deaths, $500,000 from the IRA would be distributed to the Foundation in support of Baylor’s transplant program.

Don especially liked the IRA gift idea. Always the astute businessman, he knew that leaving IRA proceeds to their children had a down side: the children would have to pay income taxes on the remaining balance in the IRA account. This tax would be in addition to estate taxes that could be imposed on that account. As a result, as much as 65% of the IRA proceeds could pass to the government, not their children. Naming the Foundation, a qualified charity, as beneficiary meant the Foundation would not pay income tax on the gift. Instead, the full amount would be designated for Baylor at the Sillers’ deaths.

Eight years after Don and Ginny set up their estate gift, Don died on November 17, 2015. He was 89 years old, and he and Ginny had been married 65 years. In January of this year, Ginny’s financial advisor, Richard Fielder with Morgan Stanley, called with an idea for Don’s IRA that could help both Ginny and Baylor.

Like all Americans over 70½, Ginny and Don are required to take annual distributions from Don’s IRA. Each year they pay income tax on the mandatory distributions. In 2015, Congress passed legislation to permanently allow Americans age 70½ or older to make direct transfers up to $100,000 from their (Continued)
Allison joined legacy Baylor Health Care System as senior executive vice president and chief operating officer in 1993 and was promoted to president and CEO in 2000. He became CEO of Baylor Scott & White Health following the 2013 merger of Baylor and Scott & White Healthcare. Over his 23 years with the organization, he has worked to grow the system from five hospitals and a few outpatient facilities in the Dallas–Fort Worth area to 48 hospitals and more than 900 patient access points across North and Central Texas. Allison’s major focus on providing high-quality care helped the organization become a nationally recognized leader in this arena. Also under his leadership, the organization created an accountable care organization (ACO)—the Baylor Scott & White Quality Alliance, now one of the largest ACOs in the country.

“There is no doubt that Joel has helped shape the health care landscape not only in Texas, but in the country,” said Jim L. Turner, chairman, Baylor Scott & White Holdings Board of Trustees. “In our national search for the next CEO, the board will be looking for someone who can continue to carry the exceptional momentum he has built. We know we are on the right course with the right strategy, and we plan to consider both internal and external candidates who are also high-integrity servant leaders.”

Investigational therapy may treat life-threatening GI leaks without surgery
Gastroenterologists on the medical staff at Baylor University Medical Center at Dallas are evaluating a new procedure for patients with gastrointestinal (GI) leaks and perforations, a complication that can result from laparoscopic surgery on the esophagus, stomach, and small intestines—and outcomes have been promising.

Steven G. Leeds, MD, medical director of minimally invasive surgery research and a gastroenterologist on the medical staff at Baylor University Medical Center, described the procedure—referred to as endoluminal vacuum (E-Vac) therapy—as “source control” for leaks that spring up in the GI tract, which can cause life-threatening infections. During the procedure, a surgical sponge is adhered to the hole in the GI tract and covered with a cellophane membrane. Negative pressure is then applied to generate inflammation between the sponge and the tissue; the inflammation expedites healing.

Dr. Leeds’ latest paper on the subject, “Endoluminal vacuum therapy for esophageal and upper intestinal anastomotic leaks,” was published online by JAMA on May 11, 2016. Coauthors are James S. Burdick, MD, and James W. Flesham, MD, also on the medical staff at Baylor University Medical Center and investigators with Baylor Scott & White Research Institute.

This procedure isn’t new—at least not in general surgery. Surgeons have used the method to promote healing for decades. It wasn’t until 2008 that researchers in Germany used this method for GI wounds. Then, in 2013, surgeons at Baylor tried the procedure on a patient who had exhausted all other options for treating an esophageal leak. By using the tried-and-true method for treating surgical wounds inside the body, researchers were able to effectively patch the hole, stop the leakage, and heal patients who were otherwise too sick for surgery.

“It actually works really well,” Dr. Leeds said. “It’s probably changed the face of how surgeons take care of wounds.” He added, “We have been able to rescue patients from hospice, accept patients from other hospitals who have had major surgical complications, and use this technique in ways it’s never been described before. In all these situations, the patients have had good outcomes and restored their ability to eat when they hadn’t been able to in the past.”

Since 2013, Dr. Leeds and fellow gastroenterologists on the medical staff at Baylor University Medical Center have performed this procedure on 46 patients, published a paper in Surgical Endoscopy (with one more pending), and presented the method at three conferences. They are creating a registry of patients who have been treated with E-Vac therapy and hope to use this data to know more about the effects and uses of this procedure. They also hope to develop an algorithm to treat more complicated leaks and introduce the method to other areas of surgery, such as transplantation, thoracic surgery, and trauma.
Cardiologist to the Mafia: reflections of a former prison doctor

John Davis Cantwell, MD

The musical *Jersey Boys*, and the subsequent movie, featured a real-life Mafia mobster and brought back memories of a time over 45 years ago when I was one of his doctors.

Desiring to get subspecialty training before entering military service, I wasn’t fortunate enough to get the Berry Plan, but did pass an exam and qualified for the Public Health Service. My top choice, the Center for Disease Control, was filled. My other options included a Leprosy Center, the Indian Health Service, and the Bureau of Prisons. I chose the latter.

I had completed a year of cardiology fellowship under Eugene Braunwald, MD, in San Diego. I was assigned to the prison hospital at Fort Leavenworth, Kansas, but petitioned to be switched to the Atlanta Federal Penitentiary (*Figure 1a*), since it was the referral center for inmates who had cardiovascular issues, given the proximity of Grady Hospital. Amazingly, my petition was accepted. I purchased a uniform and became a lieutenant commander (*Figure 1b*).

The Atlanta prison had a number of Mafia patients. Two of the most notorious were Angelo (Gyp) DeCarlo and Sam (the Plumber) DeCavalcante. I tried to take good care of the Mafia, as I like to start my car in the mornings without awakening all the neighbors.

**ANGELO DECARLO**

DeCarlo (*Figure 2*) was overweight, balding, and seemed like a mild-mannered grandfather. I never had any problems with him, nor did he ever ask me for any special favors.

I did get a glimpse of his other self one day, when I was around the corner of the hospital ward and heard him addressing another inmate. It sent chills up my spine to hear what would happen to the inmate if he crossed DeCarlo again.

In one wire tap, DeCarlo showed that he had a soft spot. A humane “hit” to him was to shoot someone in the heart, as it was a quick and relatively painless way to die.

One of my young physician colleagues, Harvard-trained and more liberal than I, seemed more involved with Gyp. One day the physician asked me to review DeCarlo’s file as it seemed to him that DeCarlo had been treated unfairly in his trial. I agreed to do so and got as far as when an informant to the FBI, Louis Saperstein, was about to expose DeCarlo, but died suddenly of arsenic poisoning.

From Piedmont Heart Institute, Atlanta, Georgia.

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DeCarlo had been diagnosed with prostate cancer while in prison, and it had spread. He learned that one could apply for parole on humanitarian grounds in the presence of metastatic cancer. One of the other doctors did the paperwork, and the parole was granted. DeCarlo told the doctor that he had made him very happy, and now Gyp wanted to return the favor by having $25,000 cash deposited on the physician’s front doorstep. The doctor assured him that he couldn’t be happier and turned down the gesture.

The pardon, by then President Richard Nixon, was questioned. One rumor involved Vice President Spiro Agnew and his friend, singer Frank Sinatra, who allegedly had ties to organized crime in New Jersey. Special Watergate Prosecutor Archibald Cox investigated the pardon and concluded that it was legitimate.

SAM “THE PLUMBER” DECAVALCANTE

I was home one night, on call for admissions to the prison hospital, and tuned into the late news. I had just heard that a notorious Mafia don, Sam “The Plumber” DeCavalcante, had been transferred to the Atlanta Federal Penitentiary when my phone rang, informing me of a new patient I needed to admit. “Is it The Plumber,” I asked? “How did you know?” was the response.

Sam (Figure 3) was a handsome man, dapper even in prison garb, with a full head of gray hair and a trimmed moustache. He got his nickname from the plumbing supply store he owned in Kenilworth, New Jersey, but preferred the nickname, “The Count,” claiming that he was a descendent of a royal family in Italy. One of the inmate nurses pulled me aside, before I started the workup, to inform me of the patient’s importance. I responded, “I don’t care if he is the president or the head of the Mafia; I try to treat them all the same.”

In the ensuing months, Sam was always cordial and never demanding. I recall once when he told me it was his son’s birthday. He had asked the boy to name any gift he wanted. His only request was for his dad to stop his four-pack-a-day smoking habit (which he did, probably one reason he lived to age 85). Like DeCarlo, DeCavalcante could turn vicious “when his authority was challenged.” In one instance, he had a fellow mobster brutally beaten when he “had failed to come in for a chat when summoned.”

FOLLOW-UP

DeCarlo died within a year or so after his parole, most likely from the metastatic prostate cancer. His burial, scheduled for an afternoon, was switched at the last minute to a quiet morning event because “the Family just didn’t want any more publicity.” When the movie about Frankie Valli and the “Jersey Boys” came out, the DeCarlo loan-shark character had a prominent role, played by actor Christopher Walken.

The DeCavalcante crime family consisted of around 60 Mafiosi. The television show “The Sopranos” was modeled after it. “The Plumber” was released from prison in 1976, 4 years after I met him, and turned control of his Mafia family over to Giovanni “John the Eagle” Riggi, in 1980. He then returned to Miami Beach, where he died in 1997 of “natural causes.”

I left the Public Health Service in 1972 and completed my cardiology fellowship training at Emory, under J. Willis Hurst. The first day of fellowship, the new doctors were asked to stand and state where they had just come from. The responses were impressive: Harvard, Stanford, Johns Hopkins, and the like. I stated simply that I had just gotten out of the Atlanta Federal Penitentiary. Everyone laughed, thinking I was joking.

Acknowledgment

My thanks to Karen Galloway for preparing the manuscript and to Stacie Waddell for doing the figures.

SOURCES

In 1934, *The Literary Digest*’s poll of the 10 most famous people in America named Franklin D. Roosevelt number one and Melvin Purvis number two. Purvis, in charge of the Chicago office of the Federal Bureau of Investigation (FBI), became famous in the 1930s for bringing down the notorious outlaws John Dillinger, Baby Face Nelson, and Pretty Boy Floyd (Figure 1).

Melvin was born in 1903 in the small town of Timmonsville, South Carolina, with a family of six sisters and two brothers. He was devoted to all his sisters, especially my mother, Callie Mims or “Cal,” who was born in 1899. In his 1920 high school yearbook, Melvin was said to be “charming and athletic with his love of horses”; he was said to be a “crack shot,” and he later became an avid gun collector. He was also popular, having been elected captain of his high school military company, and he played football and baseball in Timmonsville.

He attended the University of South Carolina and joined a fraternity, the Kappa Alpha Order. He then graduated from the University of South Carolina’s law school in 1925 and passed the bar. After practicing law for 20 months in Florence, South Carolina (10 miles east of Timmonsville), he yearned for adventure in the diplomatic service in Washington, DC. Unable to find a position in the Foreign Service, he applied at the FBI.

When Purvis joined the FBI in February 1927, it was under the strong control of John Edgar Hoover, who had been appointed the Bureau’s first director 3 years earlier. For the first 3 years of his career, Purvis worked at field offices throughout the US. In November 1930, Hoover designated Purvis special agent in charge of the Cincinnati Bureau. At the age of 27, he was the youngest field office chief in the FBI. Hoover received great reviews of Purvis, who was not only a bright man but also a hard worker and extremely attentive to details. There was no question that Purvis was a rising star.

In 1931, Purvis took over the field office in Washington, DC, and 1 month later assumed control of the Oklahoma City field office. In May 1932, Hoover made him special agent in charge in Birmingham, Alabama. At every stop, inspectors were struck by Melvin’s energy and confidence.

In 1932, Hoover’s FBI had no greater challenge than the most sinister criminals of Chicago’s underworld. To lead this dangerous time, Hoover chose his favorite agent and most dependable man: Melvin Purvis. In October 1932, Purvis was transferred to Chicago with his private secretary, Doris Rogers (later Lockerman), and made special agent in charge in Chicago. Doris Rogers called Melvin a “dapper and elegant dresser, a soft spoken gentleman, charming, young and handsome” and noted that “many of us had crushes on him then.”

Purvis later led the manhunts that tracked the most famous outlaws of all time: John Dillinger, called “America’s Public Enemy Number One,” on July 22, 1934; Pretty Boy Floyd in Ohio on October 20, 1934; and Baby Face Nelson in Illinois on November 29, 1934. Purvis had captured more public enemies
than any other agent in FBI history, in only 4 months—a record that still stands.

Reporters noted an instant liking to the modest Purvis, and the mild-mannered “G-man” became a hero and a celebrity. However, Hoover became very jealous of Purvis’s publicity. He assigned Purvis to demeaning assignments and petty criminals and later depicted Purvis as a “careless and ineffective leader.” Hoover asked that Purvis “lay low” for a few days and keep away from his office so that he would avoid the glory and attention. However, the media requested access to Purvis as well as photos of him, which were routinely denied. Finally, in December 1934, Hoover stripped Purvis of his command of the Chicago office and officially made Purvis “not in charge of the Dillinger case.” Hoover began to gather intelligence about every move Purvis made.

All of this led to Purvis’s resignation in July 1935, 1 year after the Dillinger case. Purvis moved to California, where he passed the bar and lived on Lombard Street in San Francisco. He began endorsing products such as Gillette razors and Dodge cars. He also entered into a contract with General Foods in which the Junior G-men Corps was created with badges in boxes of the popular breakfast cereal Post Toasties. In 1936, Purvis signed on to host a radio show called “Junior G-man: The Melvin Purvis Club.” The G-man Club became the most popular club of its kind, enrolling 260,000 children in the US.

Hollywood called, and Purvis was eager to serve as a technical advisor to several movies. He also briefly dated actress Jean Harlow and was a friend of Clark Gable. Later Purvis was engaged to marry Janice Jarrett, a famous advertising model best known as the Lucky Strike Girl. The wedding was planned for April 29, 1937, in San Antonio, Texas. Purvis had called and written my mother, Cal, and insisted that she and several more sisters attend. Two or three days before the wedding, he told his sisters that he was not sure he wanted to go through with the wedding. The sisters said that if he didn’t want to, he didn’t have to. The wedding was called off.

Melvin left a few days later for New York and then an extended trip to Europe. I have several letters from him to my mother, who seemed to be one of his favorites and the spokesperson for the sisters. Most of the letters were typewritten in hotel stationery but several were in longhand, which showed his incredible penmanship (Figure 2). One letter was typed from Paris on June 13th, stating that he was to travel to Berlin. This led to my first anecdote, which was an unusual encounter between Purvis and Hermann Göring.

Göring (Figure 3) was born in Germany in 1893 and was a pilot in World War I. He became a leader of the Nazi Party and was named by Hitler in 1933 to create the Gestapo, or secret
political police, and to establish concentration camps. In 1935, Göring took command of the German Air Force (Luftwaffe). Göring was fascinated with American gangsters. In 1935, he heard that Melvin Purvis was in Berlin and rang him at his hotel: “Hallo, beeg G-man,” he said. Göring then invited Purvis to his estate on a wild boar hunt.

“Carinhall” was the country residence of Göring and was built on a large hunting estate northeast of Berlin. It was named in honor of his Swedish first wife, Carin, who had died in 1931. (“Carinhall” later became the destination for many of Göring’s looted art treasures from across occupied Europe.) Göring was the master huntsman of the German Third Reich and had a singular fascination with wild boar hunting with the medieval tradition of using a spear or lance. Melvin Purvis and Hermann Göring stayed at his estate for several days, and Purvis bagged his boar and returned stateside with its tusks and hair from its neck mounted as a memento. Göring also presented him with a sword. Göring was a truly evil and ruthless man, but was one of the last great hunters in the grand tradition. He loved to share the experience of the hunt with his closest friends.

After a few months in Europe, Purvis returned stateside and made his way back West. In 1928, he returned to Florence, South Carolina, and married Rosanne Willcox, his previous sweetheart and the daughter of a prominent lawyer. He published a newspaper and started a radio station and also practiced law. Melvin and Rosanne had three sons: Melvin III, Alston, and Christopher.

The Purvises built their dream home on Cherokee Road in Florence, known as Melrose, which was modeled after a famous mansion in Natchez, Mississippi; the name had a special meaning as it was the combination of their first names. In 1940, Melvin was endorsed by a South Carolina congressman for a federal judgeship but did not get the post, as it was blocked by Hoover.

In 1942, Purvis entered the US Army as a captain and later joined the provost marshal’s office as a major. In 1944, by then a colonel and intelligence officer, he was made the deputy provost marshal general of the European Theater of Operation and had orders to interview General George Patton. Later he was made deputy director of the War Crimes Office, and after V-E day he spent time in Germany to investigate the suicide of Adolf Hitler in 1945.

A second anecdote with Hermann Göring took place in 1946, when he was a war criminal in the Nuremberg trials. Purvis was asked by the War Crimes Office to interrogate him in his cell. At first, Göring recognized Purvis and said, “Oh yes, beeg G-Man!” He asked Purvis if there was any way he could avoid execution, as he did not want to be hanged. Purvis said no. After a brief interrogation by Purvis was completed, on October 15, 1946, the night before his scheduled execution was to take place, Göring swallowed a cyanide capsule in his cell.

In the 1950s, Purvis was appointed by South Carolina Senator Olin D. Johnston as chief counsel to two Senate subcommittees. Also about this time in my teens, I would...
spend several days in the Purvis home in Florence, especially with my cousin Melvin III, who was the closest to me in age. “Big Melvin” collected guns, cars, and antiques. He was somewhat small in stature, measuring about 5’9” and 130 lbs. I would always ask Melvin about Dillinger, but he would quickly change the subject. He never talked about the FBI. He never bragged about what he had done. He had charisma and was gentle and generous, always giving us gifts after he returned from a trip.

In 1960, Purvis was suffering from very poor health. On February 29, 1960, while at his home in Florence, he died from a gunshot wound to his head fired from a pistol given to him by his fellow FBI agents in recognition of his time with the Bureau. The FBI investigated his death and declared it a suicide, although the official coroner’s report did not label the cause of death as such. A later investigation suggested that Purvis might have shot himself accidentally by cleaning his gun, trying to remove a tracer bullet that was jammed in the chamber. He was 56 years old.

In the 1990s, I planned an FBI tour while I was in Washington, DC. I told the receptionist at the FBI headquarters that I wanted to see all the information about my uncle, Melvin Purvis. The receptionist said that she didn’t know anything about Purvis and had never heard of him. I was shocked but then asked to see the exhibit on Dillinger. I could not believe that the exhibition included absolutely nothing on Melvin Purvis.

In the late 1990s, I learned that my cousin, Melvin’s middle son, Alston Purvis, was working on a book about his father’s life and wanted to stay with us in Atlanta. Alston spent several hours every day in Atlanta with Doris Lockerman, Melvin’s private secretary in his Chicago office. Even 70 years after their time together in Chicago, Doris remembered every detail of their experience in the 1930s. Doris, who was in her 90s, was a wonderful help to Alston’s project.

Alston’s book, *The Vendetta*, was published in 2005 after many years of hard work (Figure 4). Alston is an artist, author, professor, and chairman of the Department of Graphic Design at Boston University. His book is compelling, entertaining, and honest with painstaking and fascinating detail. I reread Alston’s book frequently and found it to be very useful for my article. Alston’s main focus was J. Edgar Hoover’s insane jealousy and anger against Purvis’s newfound fame and his persistent campaign to discredit and smear him. The book is really a story of changing a man from a protégé to an enemy.
Cancer Family: The Search for the Cause of Hereditary Colorectal Cancer

C. Richard Boland, MD


Reviewed by F. David Winter Jr., MD, MSc

I cannot imagine a stronger motivation to become a cancer researcher than to have most of one’s family afflicted with cancer and many of them die prematurely. Fifteen out of 23 relatives in the Cancer Family would be found to harbor a defective gene, and many would die prior to age 50 of colon or endometrial cancer.

A “tightly-knit, highly supportive” Irish-Catholic family, they grew up under a family curse. They were said to be a close family and “when they got together, there was a lot of talking, laughing, singing and obvious love and affection for one another.” However, “the one issue that was not easily discussed was cancer.” This cast a shadow over the family that influenced them in many ways. Dr. C. Richard Boland explains that there were no fights in the family and everyone got along because “they all shared a common enemy—cancer—so why waste the effort?”

Not only was the family curse a threat to their health, but the “nasty history of eugenics” made them uncomfortable talking about their pedigree. Early in the author’s research career, one of his professors, not knowing his family history, asked, “Do you think these people should be sterilized?” Controlling his anger, Dr. Boland replied, “I think that people in these families ought to be told about their possible risks, maybe preventive measures can be developed, and moreover, some people in these families might (just might) be productive in spite of their cancer risks.” He concluded the difficult conversation with an exclamation: “Also, this is my family.”

Dr. Boland did not start out to be a research scientist. He grew up in the 1960s with long hair and a healthy distrust of those in authority. A couple of innocent teenage pranks in high school, for which he was dealt disproportionate punishment, reinforced the concept. As with other pioneering scientists, most notably Albert Einstein (1), this skepticism of conventional wisdom would serve him well as he tried to untangle the family mystery.

Married while in medical school, he gives due credit to his wife for keeping him grounded and reminding him “of what things were most important.” Their decision to bear children (they would have three daughters), prior to discovery of the genetic mutation, must have led to interesting discussions.

Haunted by the death of his father to colon cancer, he did not begin his career in research until reaching the “miracle of 30.” He had actually not expected to live past his 20s. “The fact that I had reached age thirty in the context of my family history was a symbolic event for me.” Shortly thereafter, he decided to quit waiting for someone to solve the family cancer problem. His career focus shifted, and he focused on learning how to perform basic research. He found the experience humbling at first, saying that he felt he was “the dumbest guy in the room.” Thereafter, he mastered glycoproteins, learned a lot about genetics, and became an expert in oncogenes, tumor suppressor genes, and microsatellite instability. Along the way, he befriended and trained under a variety of the world’s leading scientists. Almost coincidentally, his nephew would come to play a major role in solving the family problem.

The book reads as a mystery with twists and turns along the way. As a caution to the reader, the chapters on the research studies get deep into the woods. Budding researchers and geneticists may find these sections of interest, but others are likely to be overwhelmed. However, even when discussing complicated research, Dr. Boland writes with a jocular flair. You may find his comparison of DNA sequences to Indiana Jones’ snakes fully amusing.

The story is also one of perseverance, careful observation, and deduction, though the author humbly gives equal credit to luck. He also illustrates that the pathway to success is anything but a straight line.

His scientific career shares bold experiences with other pioneering researchers. To obtain tissue for investigation, Dr. Boland “took one for the team” and was “sodomized in the name of science.” Actually, it was just a sigmoidoscopy but with a rigid scope. The lesser assaulting flexible sigmoidoscopy was just being developed by Dr. Bergein F. Overhold in 1963 and was not yet in widespread use (2).

Dr. Boland has helped to solve a horrible family affliction. He has also added to the science of genetics. Readers will find his story to be illuminating and engaging.


The reviewer, F. David Winter Jr., MD, MSc, is chief clinical officer and chairman of the board of HealthTexas Provider Network.
INADVERTENT INJECTION OF NOREPINEPHRINE, TAKOTSUBO SYNDROME, AND LOW-VOLTAGE ELECTROCARDIOGRAM

Read with interest the report by Sherif et al, published in the April 2016 issue of Proceedings (1), about the 76-year-old woman who was diagnosed with takotsubo syndrome (TS) after inadvertent injection of 4 mg of norepinephrine. The topic of iatrogenic epinephrine administration and TS was recently reviewed (2), and 3 of the 22 cases included patients who received epinephrine inadvertently for the specific drug or for a larger-than-ordered dose; in addition, another patient, not included in the review (2), who inadvertently received an infusion of 4.5 mg of norepinephrine suffered TS and subsequently received infusions of epinephrine and norepinephrine for hypotension (3). Thus, this is not the first report of TS secondary to iatrogenic norepinephrine injection, as the authors state. However, the reason for this letter is to inquire whether the low voltage of the QRS complexes, in both the limb and precordial leads, in the presented electrocardiogram (ECG) was transient, as could be ascertained by a comparison of the admission ECG with previous ECGs of the patient and ECGs recorded during her hospitalization or at ambulatory follow-up. Transient low-voltage QRS complexes in association with TS have been reported recently (4).

—John E. Madias, MD
Icahn School of Medicine at Mount Sinai, New York, NY
Elmhurst Hospital Center, Elmhurst, NY
E-mail: madiasj@nychhc.org

The authors respond:

It was a pleasure to receive a reader letter that has questions related to our recently published case report (1). I would like to clarify some points that Dr. Madias made. Dr. Madias mentioned that our case was not the first case about iatrogenic norepinephrine-induced takotsubo cardiomyopathy (TC) and referenced a review article (2). The review article concerned articles related to epinephrine induction of TC, while in our case the offending agent was norepinephrine. We agree on the similarity between these two catecholamines, but the purpose of our case report was to highlight norepinephrine as a substance that can cause this condition. In the other case report (3) that Dr. Madias mentioned, it was not clear if the patient had the diagnosis of TC, as there was no mention of whether the patient had coronary angiography to rule out coronary artery disease. Furthermore, the patient in that case report first received norepinephrine and then was later placed on both epinephrine and norepinephrine, and it was not clear if that echocardiography was done after the first exposure to norepinephrine alone or after it was combined with epinephrine. Regarding QRS voltage, the ECG on admission showed a normal QRS voltage, which might support the idea of the effect of TC on ECG voltage. Dr. Madias referred to an interesting finding in his article (4), and certainly more observational studies are needed.

—Khaled Sherif, MD, Sharmila Sehli, MD, and Leigh A. Jenkins, MD
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AN INTERESTING ELECTROCARDIOGRAM

A better interpretation of the electrocardiogram on page 165 of April’s Proceedings (Occam’s razor) (1) is type 1 second-degree heart block (Wenckebach) with intermittent A-V dissociation caused by an escape junctional rhythm faster than half the atrial rate. Complexes 8, 10, 13, 15, 18, 20, 21, and 23 are all conducted beats. The others are all junctional escape beats. The proof is in complexes 20 and 21, where there is a progressive lengthening of the PR interval in two consecutive conducted beats. When the P wave falls when the A-V node is refractory, it is conducted albeit at a prolonged A-V interval. The P-P intervals are slightly shorter when they contain a QRS complex—a known phenomenon.

—J. Edward Rosenthal, MD
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The author responds:

There is no disagreement over the interpretation. The key to understanding this rhythm is to identify the ectopic junctional pacemaker. Once that is done, the remainder is simple Wenckebach. In summary: Sinus rhythm (75 bpm) with AV block, right bundle branch block, competing junctional pacemaker (39 bpm). The easiest way to identify the junctional pacer is by its distinct cycle length.

—Howard H. McClure Jr., MD
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EFFECT OF CALORIC LABELS ON BODY MASS INDEX

Partha Deb and Carmen Vargas, both of Hunter College, focused on what happened to people’s body mass index (BMI) from 2003 to 2012 (1). They used data from the Behavioral Risk Factor Surveillance System, the annual nationally representative survey conducted by the Centers for Disease Control and Prevention (CDC) in collaboration with state health departments, to collect information on self-reported height and weight as well as demographic information. The caloric labeling in restaurants was started in New York City by Mayor Bloomberg and was required by President Barack Obama’s health care law. The men’s BMI was significantly reduced after the introduction of caloric labels. The reduction was largest among the obese (BMI >30 kg/m²), next largest among the overweight (BMI 26–30), and smallest for those with normal BMI (≤25). For women, the effect was statistically significant only for those who were overweight. These two investigators found that both men and women in the normal weight class tended to live in high-income areas and be college graduates, and the group showed little or no effect from the caloric labels. Among the men and women who showed the largest effects, an unusually high percent tended to have no education beyond high school, to be older, and to be Hispanic. These results make a lot of sense. People of normal weight have no reason to change their behavior because they do not have a weight problem. By contrast, men and women with weight problems have good reason to try to lose weight, and the labels have helped them to do just that. And if consumers are less educated, the caloric labels may be more likely to tell them something that they did not know.

US NAVY CHANGING BODY FAT REQUIREMENTS

For decades the US Navy required its men aged 17 to 39 to have no more than 22% body fat and its women of similar age to have no more than 33% body fat (2). Sailors 40 and older were allotted one additional percentage point. The number of sailors booted from the Navy annually because they did not meet these physical standards increased from 694 in 2011 to 1536 in 2014. As a result, the Navy believed it was losing too many good sailors. A change occurred in January 2016, and the new limits allow sailors to pass with a maximum 26% body fat for men and 36% for women. The Navy allowed about 2400 sailors who passed a preliminary test under the new rules to stay in the Navy. The changes are the latest by the military looking to improve its abilities to recruit and retain talented people as it builds up its cyberwarfare strategy. A 2014 Pentagon study found that roughly two-thirds of Americans would not qualify to enlist in the armed services as a result of health problems, obesity, and the failure to complete a high school education. Too bad our standards are getting more lenient.

SUPPLEMENTS

Congress lets companies market supplements without proving that they are safe and effective (3). Senior citizens are often the target. Scores of supplements promise to do away with aching joints, memory loss, and hearing problems, according to Michael F. Jacobson, PhD, the president of the Center for Science in the Public Interest. Prevagen is a synthetic jellyfish protein supplement that improves memory according to the manufacturer. Its evidence is a weak study conducted by Prevagen employees. Hawking unnecessary pills to seniors can do more than just pick their pockets. Researchers found a surprising increase since 2005 in the number of older patients who also bought fish oil when they filled a prescription for the blood thinner warfarin. It is very doubtful that supplements for arthritis or high blood pressure work and are safe. In 2015, the Food and Drug Administration (FDA) uncovered >100 supplements with “potentially hazardous” hidden ingredients. Thirty-four were “weight loss” products that were adulterated with sibutramine, a drug the agency banned in 2010 because it caused heart attacks and strokes. The US attorney general recently said, “Some of these supplements are simply a waste of money. . . . Some contain harmful ingredients causing consumers to fall ill. Others falsely claim to cure illness and disease.” She also indicated that people sometimes take worthless supplements instead of drugs that could treat their illnesses.
PREVENTING DEMENTIA

There are two major causes of cognitive decline in older people (4): 1) Alzheimer’s, accumulation of abnormal fragments of amyloid in the brain, and 2) vascular dementia, resulting from decreased blood flow in the brain. The brain’s white matter shrinks in both advanced Alzheimer’s and advanced vascular dementia. The following have been suggested as helpful in preventing dementia. 1) Prevent hypertension. There are now over 80 drugs to reduce blood pressure. The Dietary Approaches to Stop Hypertension (DASH) diet lowers blood pressure. In a 4-month intervention using the DASH diet, there were improvements in executive function, processing speed, and some aspects of learning and memory in the group that got the weight loss DASH diet and aerobic exercise. 2) Keep the blood glucose level down. Diabetes mellitus causes disease in many body organs, including the heart, kidney, eyes, and also the brain. 3) Use your brain. Live an intellectual lifestyle to delay symptoms of cognitive decline. 4) Use “brain foods.” The Mediterranean–DASH Intervention for Neurodegenerative Delay (MIND) diet is a hybrid of those two diets with a few tweaks. Instead of any fruit, for example, the MIND diet includes only berries, largely blueberries. The 10 “brain health” food groups: green leafy vegetables, other vegetables, nuts, berries, beans, white grains, fish, poultry, olive oil, and wine. The five unhealthy groups include red meats, butter and stick margarine, cheese, pastries and sweets, and fried and fast foods. 5) Do aerobic exercise 2 to 5 times a week. 6) Do strength training 1 to 2 times a week. 7) Prevent hearing loss. Hearing loss is strongly linked to a higher cognitive decline. The percentage of people with hearing loss doubles every decade. By the time they reach their 70s, nearly two-thirds of individuals have a clinically significant hearing impairment. Poor hearing may not affect blood vessels or risk of Alzheimer’s, but hearing loss may be an independent hit on the brain. 8) Stay mentally and socially active.

LEAD IN WATER

While the national spotlight focuses on the drinking water crisis in Flint, Michigan, a USA Today network investigation has identified almost 2000 additional water systems spanning all states where testing has shown excessive levels of lead contamination in the last 4 years (5). The water systems that reported lead levels exceeding Environmental Protection Agency (EPA) standards collectively supply water to 6 million people. The investigation found that at least 180 water systems failed to notify consumers about the high lead levels as federal rules require. Many of the highest reported lead levels were found at schools and daycares. A water sample at a Maine elementary school was 42 times higher than the EPA limit of 15 parts per billion, while a Pennsylvania preschool had samples that were 14 times higher. The analysis of EPA enforcement data identified 600 water systems in which tests at some taps showed lead levels topping 40 parts per billion, which is more than double the EPA’s action level limit.

Even at small doses, lead poses a health threat, especially for pregnant women and young children. Lead can damage growing brains and cause reduced IQs, attention disorders, and other problem behaviors. Infants fed formula made with contaminated tap water face significant risks. Adults are not immune. Evidence links lead exposure to kidney problems, hypertension, and increased risk of cardiovascular death. The FDA stresses that there is no safe level of lead exposure.

Most Americans get their drinking water from a fragmented network of about 155,000 different water systems serving everything from big cities to individual businesses and schools. The EPA determines that a system has exceeded the lead standard when more than 10% of the samples show lead levels >15 parts per billion. That level is called an “action level” because surpassing it requires water systems to take action to reduce contamination. Enforcement, which is implemented state by state, can be inconsistent and spotty: 373 systems have failed repeatedly, and tests continue to find excessive lead months or years later. The systems also have widely varying levels of financial resources and staff training.

The testing required by the government can include samples from as few as 5 or 10 taps in a year or even over multiple years. The system is designed only to give an indication of whether homes or buildings with lead pipes and plumbing may be at higher risk of lead leaching into the water. Even the biggest water systems in cities are required to test just 50 to 100 taps. The limited and inconsistent testing means the full scope of the lead contamination problem could be more widespread. People in thousands more communities served by water systems that have been deemed in compliance with the FDA’s lead rules have no assurance that their drinking water is safe from the brain damage toxin.

Drinking water typically is not contaminated with lead when it leaves the treatment plant. It becomes contaminated as it travels through lead service lines on individual properties and lead plumbing fixtures inside homes. At best, the EPA’s rules and testing are a sentinel system, alerting officials of the need to treat their water with anticorrosion chemicals. Doing so reduces but does not eliminate the lead in water reaching the tap.

About 75 million homes across the country were built before 1980 and are the most likely to contain some lead plumbing. That is more than half of the country’s housing units, according to the Census Bureau. The heaviest concentrations of homes with lead pipes are in New York, Rhode Island, Massachusetts, Connecticut, and Pennsylvania.

The way tap water becomes contaminated—at or even inside individual homes—poses a vexing problem for regulators, utilities, and consumers. A home with a lead service line and older internal plumbing may have high levels of lead in the tap water. A nearby newly constructed home may have no lead. The only way to know if your home is at risk is to find out about its waterline and plumbing.
Treatment of water with anticorrosion chemicals can only reduce, not eliminate, lead from leaching into tap water in invisible and tasteless doses. That’s why the EPA’s National Drinking Water Advisory Council wrote agency leaders in December 2015 calling for removal of lead service lines to the greatest degree possible. That’s a daunting recommendation since, in most cases, the water utility owns part of the line and the rest belongs to the homeowner.

CONCUSSIONS AND FOOTBALL

The National Football League acknowledged a link between concussions and the degenerative brain disease known as chronic traumatic encephalopathy (6). Chronic traumatic encephalopathy was found in the brains of 94 National Football League football players and in 45 of 55 college players whose brains were examined at autopsy. The University Interscholastic League, which governs school sports in Texas, indicated that in 2014 there were 295 football-related concussions in a statewide sample of 263 Texas schools. There were 2500 concussions related to all sports at about 40 Dallas–Fort Worth area districts in 2014 according to another investigation. According to the CDC, there are 3.8 million sports-related concussions nationwide each year. My daughter will not let her two boys, both of whom are good athletes, play football. It is understandable.

TEEN BIRTH RATE

The birth rate among American teenagers, at crisis levels during the 1990s, has fallen to an all-time low, according to an analysis for the CDC (7). The decline of the past decade has occurred in all regions of the country and among all races, but the most radical changes have been among Hispanic and black teens, whose birth rates have dropped nearly 50% since 2006. Births per 1000 females aged 15 to 90 years of age in the USA are 18 for whites, 37 for blacks, and 40 for Hispanics. Although the US has made remarkable progress in reducing teen pregnancy, too many American teens are still having babies. The birth rates for Hispanic and black teens, while lower than in the past, still are twice as high as that of white teens.

DRIVER DISTRACTIONS AND ACCIDENTS

A Virginia Tech study found that driver distractions are a significant cause of accidents (8). New technologies are adding ways to distract people. The risk of a crash caused by various distractions with a person driving while sober and paying attention is 1.0. The Virginia Tech study followed 3500 drivers in 6 states with >1600 crashes over a 2-year study period. The types of distractions and the risk number are as follows: dialing phone, 12; reading/writing, 10; reaching for object, 9; extended glance outside, 7; texting, 6; reaching for phone, 5; interacting with phone, 4; phone browsing, 3; adjusting climate controls, 2; talking on the phone, 2; overall distraction risk, 2; tuning radio, 2; eating, 2; drinking (nonalcohol), 2; interacting with passenger, 1; and managing personal hygiene, 1. Consumers, technology, and auto industry executives likely will wrestle for a long time with the trade-offs between safety, convenience, and privacy.

CAR LOCKING SYSTEMS

According to a report from Mothers Against Drunk Driving, car-locking systems have stopped about 1.8 million incidents of drunk driving since states first passed laws requiring offenders to install them in 1999 (9). The data come from the 11 main manufacturers of ignition interlock systems. The devices are wired into vehicles. A convicted drunken driver must blow into the device to get a blood alcohol content reading before the vehicle will start. The system sends a signal back to the manufacturer with the reading. Twenty-five states have laws that require ignition interlocks for all offenders following any drunken-driving offense. Every state has enacted some kind of ignition-interlock law, but some require the devices only for certain levels of offenses and blood alcohol levels or give judges discretion. Mothers Against Drunk Driving wants other states to tighten their laws.

PREDICTIVE POLICING

This policy seeks not just to fight crime but to anticipate and prevent it. It uses cutting-edge technology and big data—some from past analyses and some that stream in real time to an onboard computer in a patrol car—to identify high-risk areas, which can then be flooded with police. The aim is not to make arrests but to deter crime before it occurs (10).

Predictive policing relies on community engagement; it can work only when the police are seen as part of the neighborhood, rather than as an occupying presence. At a time when police-community relations are frayed and many cities face rising violent crime rates as well as renewed concerns about terrorist threats, the approach may provide a better way forward. Every police department in cities of 100,000 people will probably be using some form of predictive policing in the next few years.

The use of information to respond to crime has always been part of the history of policing, an essential part to solving crime after the fact. When Sir Robert Peel, Home Secretary in the early 19th century, created the British Metropolitan Police Force, nicknamed the Met, Peel had nine principles of policing that focused on the prevention of crime.

Before Peel created the Met in 1838, London was policed by the Bow Street Runners, six officers who constituted the city’s first professional police force and solved crimes as a civic service—not as professional “thief-takers” previously did, for a fee. The force was founded in 1749 by Henry Fielding, author of Tom Jones. It disbanded in 1839, the year after Peel created the Met as a civilian police presence and an alternative to a military force. The Met’s authority depended on public approval. To Peel, this meant that the police—nicknamed “Bobbies” for Peel’s first name—had to behave respectfully, succeeding not through compulsion but through the willing cooperation of citizens.

Bobbies traditionally did not carry firearms; when force was necessary, it was to be minimal. The police were not the judiciary. Bobbies did not judge guilt or innocence, did not punish or avenge. “The police are the public, and the public are the police,” Peel stated. “The Met proved itself, not by the number of criminals it caught but by the absence of crime.”
In the US, policing initially took shape along Peelian principles: cops walking the city beat deterred crime by their presence. They got to know the neighbors and the neighborhood. But after World War II the neighborhoods became less stable. In the early days of US policing, homicides were rare and few cops ever had cause to pull a gun. In New York City a weapon was drawn only in life-threatening situations, and when it was drawn it was used to “shoot to kill.”

William Bratton, who began his police career in 1970, served as chief of police in Boston, New York City, and Los Angeles, and is now again the top cop in New York City. He recently spoke of his early days as an officer in Boston, about what worked and what did not and about what can work better in the future. He indicated that now is a time of great transition. The 1960s was a time of social turbulence. Police had become reactive instead of a benign presence designed to prevent crime. They spent more and more time in their squad cars, responding to calls. At a time when people were attacking police, throwing bricks off the roofs and using guns and Molotov cocktails and fomenting revolution in the streets, patrol cars were seen as safer and more efficient. Officers could cover a greater area more quickly in a car than on foot. Random patrols and responses to calls—counterpunching—supplanted an assigned beat. It was “an ultimately damaging refocusing of the police mission and responsibility.”

The introduction of the 911 calling system reinforced the trend to reactive policing, as did a technological revolution in everything from ballistics to serology. The lab replaced the street. Suddenly, cops had a new toolbox of crime-solving techniques. Cops were more professional. There was better training, better education, and more focus on solving crime than preventing it. Now it looks like the “preventing crime” viewpoint is coming to the forefront again. If that happens there will be fewer gunshot victims in our emergency rooms.

**GENETICALLY MODIFIED ORGANISMS**

At least 64 countries require labeling of genetically modified organisms (GMOs) in food (11). American consumers now appear to be demanding GMO labeling. In the past decade, countless ballot measures and 70 bills have been introduced in >30 states to require labeling, but no bill has passed Congress. Some states have taken the issue into their own hands. In 2014, the Vermont legislature passed a law requiring GMO labeling in the state starting in July 2016. The US Congress might be stimulated to pass a national bill requiring GMO labeling if more states act. Americans have been eating GMOs for years—nearly 80% of foods contain them—with no detectable ill effects. Scientific evidence can easily fall victim to scary warnings based on emotion but devoid of fact. This explains why so many people believe that vaccines are dangerous, for example, despite exhaustive studies that prove otherwise or why people persist in believing that climate change is a hoax, despite overwhelming evidence to the contrary. The scaremongering over GMOs has been just as effective. While nearly 90% of scientists believe GMOs are safe, only 37% of Americans do. GMO critics prey on this doubt. Using science to make crops more resistant to drought or insects builds on the ancient practice of selectively breeding plants to produce better characteristics. Doing this in a lab at the genetic level makes it faster, more precise, and more effective. But it also makes the issue harder for nonscientists to grasp. That leaves a big opening for misinformation and fearmongering, which critics of GMOs have exploited to make people afraid. The facts, however, are reassuring. “The science is quite clear,” said the American Association for the Advancement of Science. “Crop improvement by the modern molecular techniques of biotechnology is safe.” And after looking at >130 research projects over a quarter century, the European Union found that GMOs are not per se more risky than conventional plant breeding.

**RUNNING BOOM OVER**

After 2 decades of furious growth in footrace participants, the number of finishers dropped 9% in 2015 compared to 2014 according to the industry-funded research group Running USA (12). The same organization indicated that the number of footrace finishers had reached an all-time peak of 19 million in 2013. Running is losing its hold particularly among 18- to 34-year-olds. Millennials, in their late teens to mid-30s, recently passed baby boomers as the nation’s largest living generation. In footraces and other running events, however, their presence is shrinking.

Most runners of course do not compete in marathons, half-marathons, 10Ks, or 5Ks. The larger pool of noncompetitive runners also is shrinking, however, especially among millennials, according to the Sports and Fitness Industry Association. Overall, the number of adults who run 50 times a year or more declined 11% from 2013 to 2015. In the same span, the total number of frequent runners, aged 25 to 34, dropped 19%. Runners aged 18 to 24 dropped 23%. That translates into about 2.5 million fewer young people who run consistently.

Millennials, however, are not sedentary. Rather, they are fueling the proliferation of studios that specialize in everything from cycling, CrossFit, and boxing to ballet barre workouts, boot camp, and weight training. Their hunger for variety is reflected in the success of ClassPass, which offers entry to a range of fitness classes in 31 US cities for a monthly fee. The service has booked 18 million reservations in less than 3 years, most of them for people in their 20s.

Millennials, according to Rachel Bachman writing in *The Wall Street Journal,* also drove the success of untimed events that are not competitive. A decrease in running will affect industry. Commercially, running is the largest US athletic footwear category by retail sales, hitting $7.1 billion in 2015, according to industry tracker SportsOneSource. Running accessories include watches, apps, and apparel. Starting and directing races has also been a fast-growing profession.

Nevertheless, running remains widely popular. It is harder than ever to get into the nation’s premier marathons—Boston, New York, and Chicago. More than 48 million people said they ran at least once in 2015. That is twice the number of people who played basketball. Among older runners in particular,
growth continues. In the last 2 years, the number of frequent runners aged 45 to 64 rose slightly while the number of those 65 and older surged 26%.

The hips and knees might be pleased with this new development, but the heart I suspect will suffer a bit.

RUNNER ED WHITLOCK

Ed Whitlock, now 85 years old, has been running since he was 40 (13). He grew up in England and later moved to Canada where he worked as a mining engineer. Over the last 2 decades, the retired engineer from Milton, Ontario, has become one of the planet’s great master runners, assembling an astonishing collection of age group world records. At age 73, for example, Whitlock ran a full (26.2-mile) marathon in 2:55 hours; at 80, he ran one in 3:16 hours; at age 85, he ran a half-marathon in 1:51 hours. These are just a few of his records. Although he does not get a thrill out of training, he runs in a cemetery near his home, small loops for hours on end. Whitlock weighs 112 pounds and stands 67 inches in height. He runs in the winter cold and in the hot summer. Ed is an inspiration to many.

WEIGHT WATCHERS ENROLLMENT UP

Weight Watchers International Inc. increased its membership rolls in the last quarter for the first time in 4 years (14). The number of active members rose 5% to 3.1 million in the quarter ending April 2, 2016, reversing a streak of quarterly declines stretching back to 2012. Thus, running is down and weight watching is up.

SEEKING MENTAL HEALTH CARE VERSUS CAREER ADVANCEMENT

The most recent health survey of US troops from 2011 shows that 37% of active-duty service members, nearly 600,000, felt that seeking mental health care through the military would probably or definitely hurt their careers. Suicides across the military rose precipitously from 2005 to 2009 and have remained at record numbers since then, according to Pentagon data and reported by Gregg Zoroya (15). The most recent suicide rate provided by the Pentagon for 2014 is 20 per 100,000. The national civilian rate for that year was 13 per 100,000, according to the American Foundation for Suicide Prevention. Posttraumatic stress disorder, depression, and traumatic brain injuries have soared in Iraq and Afghanistan. Despite a 2012 directive from the secretary of defense that seeking mental health care should not adversely impact security clearances, this practice continues. One key problem is that many Defense Department policies covering job assignments and security clearances still discriminate against anyone who receives mental health care. Troops seeking a therapist are at risk at least temporarily of losing their access to classified information.

ASSISTED DEATH BILL

Canada, in April 2016, unveiled an assisted death bill designed to ease the end of life for terminally ill patients while slamming the door on “suicide tourism” to ensure Americans and others will not flock there to die (16). People with psychiatric problems also would be excluded, and no advance consent would be allowed. The bill is now in Parliament for approval. The US states of Washington, Oregon, Vermont, and Montana also allow the practice, and California will join them in June 2016. Germany, Japan, and Columbia are among countries allowing assisted deaths. The new bill will allow Canadians to apply for a peaceful death and protect the conscience of health care providers who provide suicide assistance. The Canadian bill sets a minimum age of 18 and requires a 15-day “reflection period” to avoid quick decisions after a dark diagnosis. Patients also must be eligible for Canada’s national health care, a rule that would preclude foreigners from going to Canada to end their lives. Patients must be “suffering intolerably” and facing a “foreseeable death” to end their lives.

GROWING CHICKENS MORE SLOWLY

It is my understanding that in the USA we kill about 15 million chickens every day. According to Kelsey Gee (17), the US chicken industry has spent decades figuring out how to grow its birds faster. A typical commercial chicken has been bred to grow to twice the size of birds from 50 years ago in about half the time. The faster pace, of course, has meant big savings and fatter profits for the meatpackers that raise them. Recently, however, companies such as Whole Foods Market and Starbucks are urging producers to grow their chickens at a slower pace. Among nine chicken breeds catalogued in Gee’s article, some grow as rapidly as 28 g per day and others as much as 63 g per day. There is considerable variation in the weight of these birds at 42 days after birth: the JA57 X weighs 1057 g and the Hubbard Classic weighs 2885 g.

The growing demand for meat from animals raised more slowly reflects a broader shift in consumer taste for food and farm practices regarded as more humane and “natural.” The debate over how food should be raised has powered a flood of changes by meat companies that for decades have worked to drive down costs and scale up production. The cost of meat from slow-growing birds, which are often raised outdoors, can range from 20% to 3 times more than the price of conventional chicken raising. Most people are not willing to pay the additional cost to eat the slow-growing birds.

The breeding companies stress that the modern chicken’s feed efficiency—its ability to pack on more pounds with less feed than pigs or cattle—makes poultry ideally suited to feed a growing global population that is incorporating more protein in their diet. Global chicken production in 2016 is expected to surge to a record 90 million tons, according to the US Department of Agriculture. Some chicken breeds such as JA57 X crossbreeds reach full growth in 81 days, whereas the Rowan Ranger chickens are fully grown in roughly 56 days. Whole Foods expects its transition to selling slower-growing breeds to take roughly 8 years. It will involve repopulating farms with chickens that grow about 23% slower than the industry standard or at roughly 50 g a day. That is partly because the current supply of slow-growing birds is paltry,
with estimates ranging from <1% to 3% of commercial chickens globally. The slower-growing chickens will raise prices for consumers and use up more resources. Nevertheless, it seems like a good idea to me if one is not willing to forego chickens at all.

CLIMATE CHANGE AND WATER
The World Bank released a report in May 2016 indicating that climate change may have its greatest effect on water supplies (18). Warm temperatures cause more evaporation of water from landscapes, and changes in precipitation lead to more intense individual downpours but also swings of drought conditions. The threat affects not just what people drink but what they eat. The human activity that consumes the most water is agriculture. Then, there is the sea-level rise. It can push into coastal aquifers, as is happening in Florida, and threaten to make them more saline and less useful. The report also indicated that 1.6 billion people on Earth already live in conditions of water scarcity. Other research has put that number even higher, finding that 4 billion face conditions of severe water scarcity at least at some time of the year. The problem will be exacerbated by larger populations overall and more demand for water due to increased needs in the electricity generation and agricultural sectors. The report indicated that in the next 30 years, “the global food system will require 40 to 50 percent more water.” When water shortages happen, the poor will inevitably be hit the hardest when it comes to both food and drinking water, because they may not be able to purchase supplies from elsewhere to get them through shortages.

GLOBAL WARMING AND THE FLORIDA KEYS CORAL REEF
According to a new study (19), scientists have documented the long-term effects of ocean acidification on the coral reefs in the upper Florida Keys. This finding is called a leading indicator of climate change. The northern part of the Florida Keys reef has lost about 12 pounds per square yard of limestone over the past 6 years. Over the length of the reef, that’s more than 6 million tons!

THE PHARMACY IN THE BACK OF THE STORE
CVS Health now owns approximately 9600 in-store pharmacies, and when Walgreens and Rite Aid merge near the end of 2016, Walgreens will own nearly 13,000 in-store pharmacies (20). Wal-Mart presently has 4500 in-store pharmacies. CVS has focused on scooping up pharmacy benefit managers (PBMs), which administer prescription drug plans for health insurers and employers. The company now fills more than 20% of retail prescriptions in the USA. The theory: drive more business to the back of the store—the pharmacies that account for 67% of CVS’s revenue. They, in other words, are a combination of being both a PBM and a retail drugstore. Walgreens is equally dependent on its pharmacy business, with similar revenue coming from the back of the store. The chain has also made a big commitment to health services; Walgreens now has 400 in-store clinics nationwide. But Walgreens has largely stayed out of the PBM game. It has taken a buzz saw to costs as it expands through acquisitions. The Rite Aid acquisition should allow the chain even more buying clout and leverage with retail suppliers, although Walgreens will probably have to divest hundreds of stores to avoid antitrust concerns. These two giants will be battling for the prize of 75 million baby boomers whose spending on prescriptions and health care should steadily multiply.

MOVING TO TEXAS
Census data show that in 2015, 170,103 more residents moved into Texas from other states than left—averaging 486 new Texans each day (21)! That was the biggest gain in more than 2 decades, excluding people who left Louisiana for Texas after Hurricane Katrina in 2005. The largest number of domestic migrants came from California. Coupled with international immigration and natural population increases, domestic migration—as movement from one state to another is known—has helped propel Texas to the top of the list of the fastest-growing states over the last decade. Texas’ population grew the most of any state on average each year from 2005 to 2013—by 460,251, the state demographic report stated. California’s population increased an average of 315,043 residents every year during that period. California’s recent growth, however, has come largely through international immigration. In terms of domestic migration, California lost residents from 2013 to 2014. Texas and California are routinely the biggest trading partners when it comes to residents. In recent years, the flow of migration has shifted from Texas to California to Texas. The fact that Texas was the first state to recover from the financial meltdown in 2009 served as an incentive for domestic immigration. New residents are more likely than average Texans to have a bachelor’s degree or other higher education credentials. The fact that Texas is a more diverse economy now than in its past as a cattle and oil state can be attributed to the arrival of domestic migrants in a broad range of industries. The mean race/ethnicity percent distribution in the total Texas population as of 2013 is as follows: Asian, 4%; black, 11%; Hispanic, 37%; white, 46%; and other, 2%.

MILLENNIALS’ TOP CITY
Moving company Mayflower said that Dallas was the number 1 US city that millennials moved to in 2015 (22). Dallas surpassed Chicago, Denver, Seattle, Atlanta, Los Angeles, Portland, Charlotte, Washington, DC, and Phoenix. Most of these millennials are coming to Dallas for jobs. Since Dallas–Fort Worth is one of the top employment growth markets in the country—with more than 100,000 jobs created in the last 12 months—it makes sense that young workers would come to North Texas. Almost 80,000 people move to the Dallas–Fort Worth area each year.

DALLAS APARTMENT BUILDING
More apartments are being built in Dallas–Fort Worth than any other market in the country, and rents are at an all-time high (23). The number of units under construction
in the first quarter of 2016 in Dallas–Fort Worth was just over 43,000. In contrast, Houston has nearly 31,000 under construction; Los Angeles, 24,000; Washington, DC, 21,000; Seattle, 20,400; Denver, 19,000; Atlanta, 16,000; Austin, 14,000; and Chicago, 14,000.

PROPERTY TAXES IN TEXAS

Texas ranks as the state with the fifth highest property tax burden in the country, with a median property tax rate of 2.17% (24). The average property tax rate in Texas is about 70% higher than the nationwide average of 1.31%. Across the country, a homeowner with a property valued at $200,000 would pay $2620 a year in property taxes; in Texas, the bill would be over $4300. The four states with higher property taxes are Illinois, New York, New Hampshire, and New Jersey. The lowest property tax rates in the US are in Hawaii, the Rocky Mountain region, and southeastern states. Although the higher property taxes are offset by the lack of a state income tax, a recent study showed that Texas was among the two dozen states with the highest overall tax burden. Texas residents’ total state and local tax burden is more than 11%.

HANDWRITING VERSUS COMPUTER TYPING

Some recent studies show that handwriting appears to focus classroom attention and boost learning more effectively than typing notes on a keyboard (25). College students write about 22 words a minute and type an average of 33 words a minute. The feature that makes laptop notetaking so appealing—the ability to take notes more quickly—was what undermined learning, according to a professor at the University of Nebraska. Taking notes with a lead pencil, first mass produced in the 17th century, is not so different than using a fountain pen, patented in 1827; a ballpoint pen, patented in 1885; or a felt-tip marker, patented in 1910. Today, however, virtually all college students have portable computers, lectures are the main vehicle for instruction, and the keyboard clatter of notetaking is a sound track of higher education. Generally, students who take class notes on a laptop take more notes and can more easily keep up with the pace of a lecture than students scribbling with a pen or pencil. Researchers at Washington University in St. Louis in 2012 found that laptop notetakers tested immediately after a class could recall more of the lecture and perform slightly better than their pen-pushing classmates when tested on facts presented in class. Any advantage, though, was temporary. After just 24 hours, the computer notetakers typically forgot material they had transcribed. Nor were their copious notes much help in refreshing their memory. In contrast, those who took notes by hand could remember the lecture material longer and had a better grip on concepts presented in class, even a week later. The process of taking it down encoded the information more deeply in memory. Longhand notes were better for reviewing later points.

SINGLE LADIES

In 1877, nearly 50 years before American women were granted the right to vote, Susan B. Anthony predicted a coming “epoch of single women” (26). According to Rebecca Traister, that epoch has finally arrived. For the first time in American history, the majority of the female electorate is now composed of single women. That is the theme of Rebecca Traister’s All the Single Ladies. The book is both a sweeping history of the “invention of female adulthood” and a defense of this “new category of citizen,” whose “expanded power,” she claims, “signals a social and political rupture as profound as the invention of birth control, as the sexual revolution, as the abolition of slavery, as women’s suffrage and the feminist, civil rights, gay rights, and labor movements.”

CEO HOURLY PAY VERSUS RANK-AND-FILE HOURLY PAY

Some states presently are moving to boost the minimum wage to $15.00 an hour. The minimum wage increase will affect a large pool of workers that include store clerks, cooks, and waiters. The 76 restaurant and retail CEOs who have 2015 pay reported so far earned a median of $2700 an hour, about $5.6 million annually (27). The CEO of McDonald’s earned $3800 an hour last fiscal year, or $7.9 million. That ranked him only 25th among the 76 companies analyzed. The highest-paid CEOs in these industries had hourly pay as follows: CVS Health, $13,900; L Brands, $13,000; Starbucks, $9700; and Wal-Mart, $9300. The average CEO in the Standard & Poor’s 500 earned 204 times more than the median employee at the same companies in 2014. The Securities and Exchange Commission will soon require companies to disclose the gap between CEO and average worker pay starting in 2017.

A piece in USA Today in April 2016 (28) listed the 11 current CEOs of companies in the Standard and Poor’s 500 who in 2016 were paid at least $30 million a year. The huge amount paid to the CEOs was not proportional to how the stock of their companies did. For example, Philippe Dauman, CEO of Viacom, was paid $54.2 million in 2015 and the stock price of his company fell 44%. Mark V. Hurd and Safra Ada Catz of Oracle were each paid over $50 million in 2015 and the stock rose only 3%. Physicians are worker bees in comparison.

UNIVERSITY ENDOWMENTS

According to a piece in The Wall Street Journal, endowment assets for all US institutions in 2016 now total $529 billion (29)! The endowments in billions of the nation’s richest universities as of 2016 are the following: Harvard, $36; Yale, $26; University of Texas system, $24; Princeton, $23; and Stanford, $22. The enrollments in these five universities are as follows: Harvard, 21,000; Yale, 12,000; University of Texas system, 217,000; Princeton, 8000; and Stanford, 16,000 (dollars and numbers are rounded off). State and federal policymakers now appear to want to tax these endowments or force the wealthiest schools to spend down their endowments to defray soaring student bills and refill depleted higher education budgets.

PROLIFERATION OF ONLINE MEDICAL JOURNALS

Note: This editorial originally appeared in The American Journal of Cardiology (30) and is reprinted here with permission.
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Almost daily on my emails there is a new open access (online) medical journal requesting a manuscript from me, or asking that I review a manuscript received by them. During a recent 2-month period, I counted at least 26 heart-related journals and at least 75 non–heart-related journals (Table). Most do not have a physician as editor, and few are included on PubMed. Medicine went from having a physician editor of international distinction to a nonphysician editor of unknown qualifications. Most of the online journals charge authors to publish their manuscripts and not the readers for reading them, the reverse of hundreds of years of publishing. Some of these online journals not only request reviews from physicians of the submitted manuscripts but also request that physicians recommend names of appropriate reviewers, and some request that physicians actually manage groups of manuscripts as visiting editors. A young investigator might be tempted to submit his/her manuscript to one of the open-access journals after receiving a gracious invitation to do so rather than submit the manuscript to an established journal. I realize that online publishing without print publishing will probably be the future for most present-day print journals, but that change has not occurred yet, so I recommend staying with the print journals as long as they use that medium. Academic careers will not be built by publishing in the open access journals with nonphysician editors.

5. Young A, Nichols M. Beyond Plint: high lead levels found in 2000 water systems across USA. USA Today, March 17, 2016.
27. Krantz M. $15 an hour? Try $9,000 or more for these CEOs. USA Today, April 18, 2016.
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Submit the word processing document by e-mail to cynthiao@BaylorHealth.edu. Large files may be sent using YouSendIt or SendNow.

Cover letter and attachments: According to journal policies outlined below, list suggested reviewers and discuss potential conflicts of interest in your cover letter and provide as attachments copies of institutional review board approval or exemption, written permission for reprinting tables or figures, copies of any published material that could be considered duplicative, and release authorization forms for photographs.

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In addition to multipatient studies (original research articles), Proceedings publishes several other article types.

Case studies: The text should be no more than 5 double-spaced text pages (before the references but including the title page). Include an abstract of a few sentences, a single-paragraph introduction that explains what is unusual about this patient with this condition and thus provides a rationale for publishing the case, a case description that does not include editorial comments, a brief discussion, and up to 20 references. Case reports are not meant to be a vehicle for a literature review. Laboratory results, if extensive, may be better presented in a table instead of the text. The maximum number of figures and tables (combined) is 5. Please crop images, add arrows as needed, and include descriptive legends.

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Reader comments (letters to the editor): Both responses to previously published material and brief reports or observations are considered for this section. The limit is 1200 words.

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Format: Type manuscripts double spaced, leaving 1-inch margins. Number all pages, including the title page. Indent paragraphs. Start the first paragraph of the text and the beginning of the reference section on a new page and place figures on separate pages.

Title page: Include on the first page the article’s title; the authors’ first names, middle initials, and last names with highest degree(s), listed in a single row; a summary of authors’ affiliations, with departments, institutions, cities, and states; and the name, address, e-mail address, and phone number of the corresponding author. Acknowledge any grant support.

Abstract: Provide a one-paragraph double-spaced abstract of 150 to 250 words. Abstracts are required for original articles and case studies and are recommended for reviews and long historical articles.

Conclusions: Conclusion paragraphs at the end of the discussion section are rarely needed and are often cut if included.

References: Number references according to the order in which they are cited in the text and type them double spaced at the end of the manuscript. Do not use the footnote or endnote functions of word processing software. The numbers in the text should be on line and in parentheses, such as (14, 16, 17). The references should conform to the following style, listing all authors:


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Use of color: Authors are asked to pay $100 for each color figure or table. Generally, color is suggested only when clinically required (as with certain pathology and radiology images). Avoid using color when creating charts and graphs. If photographs (such as those in...
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— A single-paragraph abstract of 150 to 250 words is included. For case studies: After the abstract, the manuscript includes a single-paragraph introduction, and the page count before the references is no more than 5 double-spaced pages. The manuscript does not exceed the limit of 20 references or 5 figures and tables.

— Figures are high-resolution. Photographs are 350-ppi tiff or jpeg files.

— References include all authors, the full article title, the journal abbreviation from *Index Medicus*, the volume and issue number, and inclusive page numbers. References in the text appear in parentheses, rather than in superscript or footnotes or endnotes.

— All authors have approved the version to be submitted.

Manuscripts that do not meet these requirements may be returned to authors before peer review is initiated.
Baylor University Medical Center Proceedings

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