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<th>Research area</th>
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<td>Rose Boehm, CCRC, RRT, RCP</td>
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<td>Jana Holloway, RRT, CRC</td>
<td>214-820-9772</td>
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<td>and head and neck cancer, hematological malignancies, leukemia, multiple myeloma, non-</td>
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Baylor Research Institute is dedicated to providing the support and tools needed for successful clinical research. To learn more about Baylor Research Institute, please contact Kristine Hughes at 214-820-7556 or Kristine.Hughes@BaylorHealth.edu.
Use of the bootstrap method to develop a physical fitness test for public safety officers who serve as both police officers and firefighters

Jenny Adams, PhD, Dunlei Cheng, PhD, John Lee, BS, EMT-P, Tiffany Shock, BS, Kathleen Kennedy, MS, and Scotty Pate, RT(R)

Physical fitness testing is a common tool for motivating employees with strenuous occupations to reach and maintain a minimum level of fitness. Nevertheless, the use of such tests can be hampered by several factors, including required compliance with US antidiscrimination laws. The Highland Park (Texas) Department of Public Safety implemented testing in 1991, but no single test adequately evaluated its sworn employees, who are cross-trained and serve as police officers and firefighters. In 2010, the department’s fitness experts worked with exercise physiologists from Baylor Heart and Vascular Hospital to develop and evaluate a single test that would be equitable regardless of race/ethnicity, disability, sex, or age >50 years. The new test comprised a series of exercises to assess overall fitness, followed by two sequences of job-specific tasks related to firefighting and police work, respectively. The study group of 50 public safety officers took the test; raw data (e.g., the number of repetitions performed or the time required to complete a task) were collected during three quarterly testing sessions. The statistical bootstrap method was then used to determine the levels of performance that would correlate with 0, 1, 2, or 3 points for each task. A sensitivity analysis was done to determine the overall minimum passing score of 17 points. The new physical fitness test and scoring system have been incorporated into the department’s policies and procedures as part of the town’s overall employee fitness program.

The physical demands of police work and firefighting are well documented (1, 2), as are the low fitness levels (3, 4) and high rates of morbidity and mortality from cardiovascular disease that are often associated with these occupations (1, 5). In theory, physical fitness testing is a straightforward and logical way of motivating public safety personnel to reach and maintain a minimum level of physical conditioning so they can perform arduous job tasks. In practice, however, choosing and implementing a physical fitness test at an individual work site can be highly problematic: Such tests must comply with US laws that prohibit discrimination on the basis of race, color, religion, national origin, sex, age, or disability (6), characteristics that define protected classes. The Highland Park Department of Public Safety (HPDPS), in the town of Highland Park, Texas, is unusual because it employs public safety officers who are cross-trained as firefighters and police officers. For over a decade, the department used two kinds of fitness tests simultaneously (a general test consisting of exercises such as push-ups, sit-ups, and running and a task-based test consisting of firefighting activities), but providing both was costly, time consuming, and cumbersome. In 2010, exercise physiologists from Baylor Heart and Vascular Hospital who are familiar with the functional capacity requirements for firefighters and police officers (7, 8) began working with fitness experts from HPDPS in a study to develop and evaluate a single, equitable test that would meet the department’s unique requirements. This article describes that collaboration and the results it yielded.

METHODS

Baylor Research Institute’s institutional review board approved the study, and all 50 subjects (all of whom were sworn employees of HPDPS) gave informed consent and provided demographic information. Data were collected on the 45 men and 5 women (aged 23 to 61 years; mean, 41 years) during a series of three quarterly testing sessions. The timed obstacle course comprised 10 activities and was divided into three sections. The first section, general fitness, evaluated agility with the Illinois test, flexibility with the sit and reach test, and muscular endurance with push-ups and sit-ups. The remaining sections evaluated muscular strength and cardiovascular fitness through a series of job-specific tasks related to firefighting (stair climbing, ceiling breach, and forcible entry) and police work (chasing, fighting, and handcuffing a perpetrator) (Figure 1). While the test was being developed, the subjects did two trial runs, enabling the study staff to fine-tune various aspects of administering the test.
test before collecting data. The assumption was made that the employees’ job performance was above average at the time of testing; therefore, only their data would be used to derive the grading criteria and minimum passing score.

Testing took place at HPDPS headquarters and was monitored by the study staff and by HPDPS peer fitness coordinators. Paramedics and a mobile intensive care unit were available in case of an emergency. The subjects wore athletic apparel (shorts, t-shirt, and athletic shoes) and were given detailed instructions before and during the test. They were asked to complete the following tasks, in order, as efficiently as possible:

- **Illinois agility test.** From a prone position on the floor with outstretched hands placed behind the starting line, the subjects rose and sprinted (straight and serpentine) through a series of cones as fast as possible. (Recorded value: total time.)

- **Push-ups.** For 60 seconds, the subjects performed as many consecutive full-body push-ups as possible, touching their chest to a commercial push-up counting device when in the down position to ensure consistency. (Recorded value: number of repetitions.)

- **Sit and reach test.** The subjects, without shoes, sat on the floor with their legs extended and the soles of their feet against the edge of the testing box, which had a scale and a metal slider on top. With their arms evenly stretched, hands parallel, and palms down, they slowly reached forward as far as possible, pushing the slider along the scale. (Recorded value: longest reach during three attempts.)

- **Sit-ups.** With bent knees, fingers cupping the ears, and ankles held firmly by a partner for support, the subjects performed as many sit-ups as possible in 60 seconds. (Recorded value: number of repetitions.) The subjects were given a 2-minute rest before continuing to the firefighter tasks.

- **Stair climbing.** While wearing a 50-pound weighted vest with an additional 12.5-pound weight on each shoulder, the subjects performed a 20-second warm-up on a stepping treadmill at a rate of 50 steps per minute. They were then timed while stepping at a rate of 60 steps per minute for up to 3 minutes. (Recorded value: actual time at 60 steps per minute.)

- **Ceiling breach.** The subjects removed a 5-pound pike pole from a bracket and placed the tip on the 60- to 80-pound push/pull pike pole simulator. They attempted to complete 3 sets, each set consisting of 5 pulls and 3 pushes. (Recorded value: number of completed sets.)

- **Forcible entry.** While standing on steel planks alongside a 160-pound beam, the subjects slammed a 9-pound sledgehammer into the end of the beam until either the beam moved 5 feet or the 60-second time limit ended. (Recorded value: movement of the beam in thirds.) The subjects were given a 2-minute rest before continuing to the police tasks.

- **Perpetrator takedown.** The subjects a) sprinted 300 yards; b) participated in a mock fight by delivering a series of 24 punches to a target dummy; and then c) dropped to their knees on a mat, rolled a 150-pound dummy four times one way and four times back, and simulated a behind-the-back handcuff by bringing the dummy’s hands together behind its back. (Recorded value: total time.)

The raw values collected during the three quarterly testing sessions were analyzed to determine the appropriate ranges for a scoring system that would assign 0, 1, 2, or 3 points for each task, according to level of performance. The bootstrap method was used; it was introduced in 1979 as a novel statistical technique that falls under the broad heading of resampling. When a statistic such as the sample mean is computed on a data set, that single statistic is known but its variability is not. Through resampling, the bootstrap method creates a larger number of data sets and computes the statistic on each of them. Thus, a distribution of the statistic is obtained, permitting an estimate of the statistic afterwards. The bootstrap technique involves many repetitions of a relatively simple procedure and is heavily dependent upon computer calculations.
In the present study, bootstrapping was used to first obtain a mean distribution of each of the test categories. The derived bootstrap distribution was then used to find the values at 2.5% (1 point) and 97.5% (3 points). The values between those for 1 point and 3 points defined the range for 2 points. The values for 1 point defined those for 0 points (e.g., if 10 to 31 sit-ups = 1 point, then <10 sit-ups = 0 points). Figure 2 includes the histogram of the raw Illinois agility test values and the histogram of the mean distribution of such values via bootstrapping. Although the recorded values are right skewed, the derived mean distribution is quite normal after resampling 10,000 times.

After all the subscores for each item were added, a sensitivity analysis was done to determine the appropriate minimum passing score. Ranges of scores were chosen to ensure that 80% or more of the protected class (defined for this study as racial or ethnic minority, disabled, female, or age >50 years) would be able to pass the test (10). Overall scores for the physical ability test were compiled by summing all points achieved during each test component, and the minimum passing score was 17 points. All analyses were done with R 2.14 software (R Project for Statistical Computing, http://www.r-project.org).

Finally, HPDPS leadership worked with the town council, town administrator, human resources staff, and legal counsel to develop a long-range plan for implementing the new testing procedure.

RESULTS

The new physical fitness test and scoring system, summarized in the Table, have been incorporated into the policies and procedures of HPDPS as part of the town’s overall employee fitness program. All sworn employees are required to exercise regularly while on duty (as emergency calls and other responsibili-

Figure 2. Histograms of (a) the raw values from the Illinois agility test and (b) the mean distribution of the raw values through bootstrapping.

DISCUSSION

Reaching and maintaining an adequate level of fitness is a key component of maintaining job readiness, and physical fitness testing can play an important role. The goal of achieving fairness in physical fitness testing remains elusive (11), however, and employers’ use of such tests has been hampered by many factors, including fear of legal action, complaints by employee groups, and lack of funds (10). Various tests have been used in the past and are still used, but they have been challenged
repeatedly. For example, it can be difficult to show that the exercises long used for general fitness testing are essential to a specific job (11). Task-based tests, such as climbing a fence or dragging a dummy, simulate job activities but often discriminate against women, minorities, and people who are older or disabled.

Despite these problems, physical fitness testing is a necessary tool in the public safety workplace. Fire departments seeking to implement a task-based test can choose from protocols that are commercially available but often very expensive to license or administer. Police departments, which have fewer testing options to choose from, tend to use activities from the general fitness category. Because no existing test adequately addressed the combined police officer/firefighter job description at HPDPS, the leaders chose to develop a new test to meet the department’s nontraditional needs.

To determine a scoring system that would be fair, the bootstrap method was used to compare raw data from all employees who took the test, including those who were in the protected class. The resulting scoring criteria, determined solely from this group of subjects, allow for differences in skill levels while encouraging improvement. In the past, a task such as dragging the dummy was graded as pass or fail. In the new test, dragging the dummy one third of the total distance earns 1 point, which could motivate the employee to perform better in the future instead of giving up on the task completely.

Because this study involved a specific cohort of sworn officers in a single public safety department, the results (particularly the scoring system) are not generalizable to other police or fire departments. However, the structure and organization of the HPDPS test, along with the bootstrap method described herein, could benefit other departments that seek to develop a customized physical fitness test.

For more than 3 decades, disputes over the fairness of fitness standards in the US workplace have led to hundreds of legal actions, costing taxpayers millions of dollars. Even the fear of being sued has had a paralyzing effect on some employers, causing them to abandon physical fitness tests and standards entirely (10). These concerns, however, have not deterred HPDPS from its current goal of motivating sworn employees to improve and maintain their level of fitness and overall wellness. The present study produced the new testing procedure and scoring criteria that are being used to support that goal.

Acknowledgments

We thank the Highland Park (Texas) Department of Public Safety for participating in this study. We also thank Beverly Peters, MA, ELS, for help in developing and preparing the manuscript.

Growing evidence shows that early mobilization of patients in the intensive care unit (ICU) is a safe and cost-effective strategy to improve patient outcomes. However, in ICUs where early mobilization has not been practiced, its adoption requires culture change by the multidisciplinary team, including physical therapists, nurses, respiratory therapists, and physicians. We describe a physical therapist–led program to introduce such changes in a medical-surgical and a cardiovascular ICU. Interdisciplinary and multidisciplinary meetings and education sessions informed critical care team members about early mobilization and encouraged knowledge sharing for safety and effectiveness. A lead physical therapist was appointed to advocate for early mobility and developed solutions to overcome the identified barriers. After the initiation of this program, the number of ICU patients receiving physical therapy evaluations increased from 364 in 2011–2012 to 542 in 2012–2013. In this article, we describe our experience from 21 patients who underwent early mobilization. A physical therapist–led initiative can help establish an ICU culture that supports early mobilization, but the change is slow and requires interdisciplinary collaboration to identify and overcome barriers.

METHODS

Baylor All Saints Medical Center at Fort Worth is a 525-bed acute care hospital in Fort Worth, Texas. It is a private, not-for-profit, urban, full-service hospital, providing a broad range of medical services, including cardiology, transplantation, neurosciences, oncology, and women’s services. The facilities include a 16-bed medical-surgical ICU and a 15-bed cardiac ICU in which the patient-to–registered nurse (RN) ratios are maintained at 1:1 or 2:1. The ICU has several intensivist groups, most of whom are pulmonologists. The specialties include neurosurgery, cardiovascular surgery, head and neck reconstruction surgery, and liver and kidney transplantation. The patient population in the ICU and cardiac ICU includes those with diagnoses such as pneumonia, sepsis, respiratory failure, diabetic ketoacidosis, myocardial infarction, heart failure exacerbations, and chronic obstructive pulmonary disease. One internal medicine physician rounds on all reconstructive head and neck patients. The PTs and RTs are contractors, and the nurses are staff. There is not a hierarchy among these disciplines.

Prior to implementation of this program, there was no protocol for ordering physical therapy for patients admitted to the ICUs. Rather, physical therapy orders were handled on an ad

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h oc basis. After receiving the orders, the PT performed chart reviews and contacted the nurses to determine if the patients were stable to participate in physical therapy services, using guidelines taken from a combination of nursing education courses the lead PT attended as well as literature and continuing education courses attended. These guidelines included a heart rate of 40–130 beats per minute; a systolic blood pressure < 180 mm Hg; a mean arterial pressure > 65 mm Hg; mechanical ventilation < 100 mm Hg; pulse oximetry > 88%–90%; respiratory rate < 40 breaths per minute; mechanical ventilation settings of fraction of inspired oxygen < 0.60 and positive end-expiratory pressure < 10; as well as alertness, ability to follow commands, and lack of agitation.

If a patient met these guidelines, he or she was evaluated and received physical therapy 3 to 5 times per week. Patients who were not stable enough to participate were assessed daily to determine their eligibility for participation in physical therapy. Physical therapy sessions were based on both the patients’ previous level of function and their ability to participate on the day of the treatment session. Accordingly, exercises could be performed in the supine or chair position in bed, sitting on the edge of the bed, in the chair beside the bed, or standing. Figure 1 outlines the progression.

In May 2011, the physical therapy department initiated steps toward introducing early mobilization as standard practice in Baylor All Saints ICUs after a PT began to notice discrepancies in evidence and what was being practiced in the ICU. The PT found that it was acceptable to progressively mobilize patients who had undergone coronary artery bypass graft surgery but not other patients who seemed to meet criteria to participate in PT services. Often these patients were not even receiving orders for PT. Recognizing the importance of interdisciplinary communication and collaboration for early mobilization, the focus was on establishing a culture to support this goal, while simultaneously educating physicians, nurses, RTs, and PTs on both the benefits of early mobilization in the ICU and on factors within each other’s domains that needed to be considered in relation to mobilization of critically ill patients.

We began by inviting the ICU nurse manager to our departmental meeting, who then invited us to the critical care quality meetings. We attended one critical care quality meeting and at the next meeting presented early mobility information. While continuing to attend the critical care quality meetings, we invited other team members to our departmental meetings. We held 3 meetings over a 6-month period and included the cardiac ICU nurse manager, who provided education on reading electrocardiography strips and the more common complications seen on the unit and answered questions about the equipment commonly in use in the cardiac ICU, critical lab values that needed to be considered in evaluating patients’ readiness for mobilization, and perceived contraindications to activity/mobilization. Also present was an RT, who provided education on the different oxygen delivery devices used in the ICU and the ways they could be adjusted or converted for activity/mobilization. Additionally, there was a critical care nurse, who provided education on continuous dialysis and answered questions about mobilizing patients while they were on these machines.

Two months later, PT team members were invited to attend the monthly hospital critical care quality meetings and to provide education on early mobilization in this forum. As regular attendees of the meeting included an intensivist, nurse managers of both the medical-surgical and the cardiac ICUs, the hospital’s critical care director, the respiratory therapy manager, and a nursing representative, PTs took this opportunity to educate the group on the existing evidence of the feasibility of and benefits associated with early mobility in the ICU.

Additionally, we organized phone conferences with other physical therapy departments within the hospital system to determine what the other facilities, namely Baylor University Medical Center at Dallas, Baylor Regional Medical Center at Grapevine, and Baylor Medical Center at Garland, were doing in their ICUs regarding mobility. Based on the information gathered, we made two important changes to our own department’s functioning to better facilitate our aim of promoting early mobilization in the ICU. First, we stopped automatically placing patients transferred to one of the ICUs from the step-down units on a physical therapy “hold,” which meant we would wait for new orders from the physician. This was done after discussions with the PTs, nurses, and physicians revealed that some of the physicians were not aware that was the practice. One of the primary intensivists stated that he expected the therapists and nurses to discuss the case and make a clinical judgment about whether the patient could continue to participate. Second, we designated a lead PT for critical care. Third, the lead PT instituted ad hoc meetings with the ICU nurse managers in addition to the respiratory therapy manager, both

<table>
<thead>
<tr>
<th>Patients are placed in the chair position in bed to improve ventilation and orthostatic conditioning.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who are able to tolerate the chair position in bed progress to sitting on the edge of the bed, followed by standing at the edge of the bed with or without a rolling walker.</td>
</tr>
<tr>
<td>Patients who are able to stand and pick up their feet are transferred to a chair, or, if able, ambulate.</td>
</tr>
<tr>
<td>Patients who are unable to bear weight through their lower extremities or sit on the edge of the bed might be transferred passively to a neuro chair if deemed appropriate.</td>
</tr>
</tbody>
</table>

Figure 1. Progression of physical therapy exercises for patients in the intensive care unit.
together and separately, to provide further education on the importance of early mobility and gain their support. It was communicated to the managers that PTs often met resistance from nursing to provide interventions. The need to have PTs, RNs, and RTs work as a team to determine appropriateness for mobility and any needed oxygen or medication changes, i.e., decreasing sedation, changing the timing of pain medication, and increasing oxygenation support, was discussed in these meetings.

The meetings with the RTs and nurse managers focused on advocating early mobilization and the importance of collaboration across the entire critical care team in this process. We also discussed the changes made within the physical therapy department related to facilitating early mobilization and discussed the perceived barriers that were encountered.

Additionally, the lead PT was tasked with attending the multidisciplinary ICU rounds thrice weekly to advocate for early mobilization, request physical therapy orders for patients, and answer any questions the critical care team had about early mobilization. The lead PT also sought out and attended continuing education courses provided through various PT continuing education providers and taught by published, experienced critical care PTs. The courses provided information that was relevant to safely mobilizing ICU patients attached to multiple lines such as the ventilator, continuous dialysis, femoral lines, and arterial lines, as well properly monitoring their vital sign response to the dosage of activity. This material was passed on to the other PTs during the monthly critical care meeting we instituted in our department to review updates from the critical care quality meetings. The lead PT also provided education at critical care nursing staff meetings and nursing internship courses. The information addressed both the evidence supporting early mobilization in the ICU and the practical matters of when physical therapy orders should be requested, as well as what the PT was assessing/targeting when evaluating and treating a patient. Participation in all education sessions was voluntary.

During the middle of this process, the lead PT conducted an anonymous e-mail survey of the critical care nursing and respiratory therapy staff to identify their concerns regarding any perceived barriers to early mobility in the ICU, as well as opportunities to improve the quality of care the physical therapy department could address. The 9-question survey, which included yes/no questions and open-ended questions (Table 1), was administered to build an open culture of communication and collaboration. It enabled the PT to demonstrate to the ICU managers and RT managers that there were still issues that needed to be addressed to accomplish early mobility in the ICUs.

Finally, in conjunction with our efforts to promote early mobility in the ICU, we reviewed a convenience sample of 21 charts for patients who had an ICU stay of 3 days or longer between May 2012 and May 2013 and who participated in physical therapy sessions in the ICU. The purpose of this review was to gain a sense of the characteristics of the patients receiving physical therapy interventions in the wake of our efforts to promote early mobilization in the ICU, as well as of the type of physical therapy intervention appropriate for these patients.

Table 1. Survey questions

<table>
<thead>
<tr>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you think physical therapy should evaluate/screen all intensive care unit/cardiovascular intensive care unit patients?</td>
</tr>
<tr>
<td>2. Do you feel comfortable getting patients into neuro chairs without physical therapy?</td>
</tr>
<tr>
<td>3. Do you feel comfortable using the mechanical lifts without physical therapy?</td>
</tr>
<tr>
<td>4. Do you get patients out of bed/ambulate without physical therapy if they are able?</td>
</tr>
<tr>
<td>5. Do you think patients should be getting up on ventilators?</td>
</tr>
<tr>
<td>6. What are the barriers to mobilizing patients on ventilators?</td>
</tr>
<tr>
<td>7. What are the harmful effects of physical therapy working with patients in the intensive care unit?</td>
</tr>
<tr>
<td>8. What can physical therapy do to improve communication with the RNs, MDs, respiratory therapists, patients, families, etc.? Please be specific.</td>
</tr>
<tr>
<td>9. What can physical therapy do to improve patient care? Please be specific.</td>
</tr>
</tbody>
</table>

We excluded patients who had head or neck reconstructive surgery as well as those who were discharged to hospice or died during their hospitalization. All data—including the number and type of physical therapy sessions, patient demographics, diagnoses, and clinical characteristics—were extracted from the electronic medical record and entered manually into a database created for this purpose. We also examined the total number of physical therapy evaluations performed on ICU patients during the first (April 2011–April 2012) versus the second (May 2012–May 2013) years of our intervention to determine if the number of PT orders had increased after some of the initiatives were implemented.

RESULTS

Findings from the shared meetings showed that inviting members of the critical care team to share their knowledge with the physical therapy department opened the door to the interdisciplinary communication and collaboration needed to support early mobilization in the ICU. The meetings also provided an important opportunity for members of the physical therapy department to raise any questions or concerns they had related to early mobilization in the ICU with the experts best able to address them. For example, we discussed whether there were policies against mobilizing patients with certain lines such as femoral or Quinton catheters as well as critical lab values that may affect PT interventions. In addition, we learned that often we were limiting our patients’ mobility based upon outdated notions rather than current evidence. For example, in one instance, a PT did not see a patient because his potassium was critically low. Subsequently, the nurse manager educated the team that we should ask the nurses if the patient is receiving a K+ rider because, in most instances, the potassium had been replaced since that lab value was drawn. From findings from the phone conferences with the other physical therapy departments in the Baylor system, it was determined that there was a benefit in having
a dedicated ICU therapist because this helped to build trust and confidence with the nursing and RT staff. It was also found that the other facilities utilized a tech more frequently to assist with treatments. Specifically, this led us to designate a critical care lead PT who was able to devote time to learning more about safely providing physical therapy in this context and to representing the physical therapy department and advocating for early mobilization at the critical care quality meetings and interdisciplinary rounds. We also changed department policy to stop placing patients participating in physical therapy on automatic hold if they were transferred to one of the ICUs.

Furthermore, in other findings, the results of instituting meetings with the respiratory therapy and critical care nurse managers led to the identification of important perceived barriers. During these meetings, the PT discussed with the managers the barriers to early mobilization, which included the nursing staff being resistant to PTs getting patients out of bed, working with patients who had multiple lines, and scheduling mobility with RTs and RNs when the patient was on a ventilator. The meetings were beneficial because the managers felt early mobility was important and were able to relay this message to the nursing and RT staff, resulting in a collaborative effort.

Survey results from 32 RTs and nurses uncovered some additional perceived barriers as well as some opportunities for improvement. Barriers that individuals indicated on the survey included the severity of patients’ illness, safety concerns, time constraints, staff shortages, fear of pulling out lines and tubes, and the need for culture change. All respondents agreed that all ICU patients should be evaluated by PT. Twenty-eight percent of the respondents indicated that patients should mobilize on ventilators but cited the barriers mentioned above. It was determined after reading some of the responses to the survey that ongoing education needed to be provided, not only to address the barriers but also to inform the nursing staff of the role of physical therapy and the type of education we have. An interesting finding was that often the nurses felt as though PT was not progressing the patients adequately.

Results from our review of the 21 patients who participated in physical therapy in the ICU are shown in Tables 2 and 3. From April 2011 to April 2012, 364 physical therapy evaluations were performed on patients admitted to the ICU. From May 2012 to May 2013, this number increased to 542.

**DISCUSSION**

The physical therapy department at Baylor All Saints Medical Center at Fort Worth initiated and led a series of education sessions and discussions intended to establish a culture of interdisciplinary communication and collaboration to support the use of early mobilization in its medical-surgical and cardiac ICUs. Through these efforts, we identified important perceived barriers and concerns about early mobilization (e.g., concerns for safety with critically ill patients who have multiple lines, having enough staffing, needing multidisciplinary collaboration, and accounting for educational needs and the time required) across multiple disciplines, which we were able to start addressing through education and training involving nurses, RTs, PTs, and intensivists.

Previous studies have shown early mobility protocols to improve ICU patients’ outcomes and decrease the costs associated with their care (4–6, 12). They have also identified barriers at the organizational level to implementing early mobility protocols, including a need for both institutional and project leadership; additional staffing and equipment; increased physician referrals for physical therapy closer to patient ICU admission; and management of patients’ pain, delirium, and tolerance for activity and safety (13, 14). We examined the perceived barriers and concerns from the perspective of the frontline critical care staff—nurses, RTs, and PTs. The barriers found here were similar to those described in other research, including staffing needs and multidisciplinary collaboration, but also included safety concerns, educational needs, and the amount of time it takes to mobilize patients on multiple lines (12, 15, 16).

Our review of the 21 patients who participated in physical therapy sessions in the ICU provides other physical therapy departments that want to implement an early mobility program some idea of the kinds of patients and the type of session they can expect. Significant proportions of the participating patients were on ventilators or continuous dialysis, meaning

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**Table 2. Characteristics of 21 randomly selected patients who participated in physical therapy sessions in the medical-surgical or cardiac intensive care unit between May 2012 and May 2013**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>60.4 ± 15.4</td>
</tr>
<tr>
<td>Male</td>
<td>10 (48%)</td>
</tr>
<tr>
<td>Ventilator</td>
<td>12 (57%)</td>
</tr>
<tr>
<td>Non-Hispanic Caucasian</td>
<td>12 (63%)</td>
</tr>
<tr>
<td>Body mass index, mean ± SD (kg/m²)</td>
<td>30.0 ± 12.7</td>
</tr>
<tr>
<td>Insurance</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>12 (57%)</td>
</tr>
<tr>
<td>Private</td>
<td>9 (43%)</td>
</tr>
<tr>
<td>Admitting unit</td>
<td></td>
</tr>
<tr>
<td>Intensive care unit</td>
<td>9 (43%)</td>
</tr>
<tr>
<td>Cardiovascular intensive care unit</td>
<td>12 (57%)</td>
</tr>
<tr>
<td>Days in hospital, median (IR)</td>
<td>10 (6, 18)</td>
</tr>
<tr>
<td>Days in ICU, median (IR)</td>
<td>9 (5, 18)</td>
</tr>
<tr>
<td>Able to ambulate prior to ICU admission</td>
<td>17 (81%)</td>
</tr>
<tr>
<td>Severity criteria as of day 3 of ICU stay</td>
<td></td>
</tr>
<tr>
<td>On a ventilator</td>
<td>7 (33%)</td>
</tr>
<tr>
<td>Postoperative</td>
<td>7 (33%)</td>
</tr>
<tr>
<td>Received continuous renal replacement therapy</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>On a vasopressor</td>
<td>9 (43%)</td>
</tr>
<tr>
<td>Unable to follow commands</td>
<td>5 (26%)</td>
</tr>
</tbody>
</table>

ICU indicates intensive care unit; IR, interquartile range; SD, standard deviation.
that PTs need to plan for sessions that accommodate the restrictions these pieces of equipment impose. We also found that most patients were able to participate in at least some sessions sitting on the edge of the bed or standing next to the bed; a surprising proportion were also able to transfer to a chair or ambulate during some sessions. Through this process, it was found that if given the time for the patient to adjust to positional changes such as supine to sit, sit to stand, and so forth, these patients could progress further and tolerate more activity. This is important information, as PTs unfamiliar with the critical care setting might be hesitant to conduct such sessions, and while caution is obviously the watchword in this context, in achieving the full benefits of early mobility, avoiding “underchallenging” patients might be almost as important as avoiding “overchallenging” them.


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**Table 3. Characteristics of physical therapy sessions conducted with the 21 randomly selected patients who participated in physical therapy sessions in the medical-surgical or cardiac intensive care unit between May 2012 and May 2013**

<table>
<thead>
<tr>
<th>Description</th>
<th>Any episode</th>
<th>Median (IR), if any</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration in minutes, median (IR)</td>
<td>–</td>
<td>49 (35, 80)</td>
</tr>
<tr>
<td>Median total number of physical therapy sessions (IR)</td>
<td>–</td>
<td>2 (1, 3)</td>
</tr>
<tr>
<td>Day of first exercise session after critical care admission</td>
<td>–</td>
<td>3 (2, 6)</td>
</tr>
<tr>
<td>Episodes of passive range of motion (patient did not participate)</td>
<td>3 (14%)</td>
<td>1 (1, 6)</td>
</tr>
<tr>
<td>Episodes of active exercise sessions with lower extremities</td>
<td>9 (43%)</td>
<td>2 (1, 3)</td>
</tr>
<tr>
<td>Episodes of sitting on edge of bed</td>
<td>16 (76%)</td>
<td>1 (1, 2)</td>
</tr>
<tr>
<td>Episodes of standing</td>
<td>15 (71%)</td>
<td>1 (1, 2)</td>
</tr>
<tr>
<td>Episodes of transferring to chair by weight bearing through lower extremities</td>
<td>8 (38%)</td>
<td>1 (1, 1.5)</td>
</tr>
<tr>
<td>Episodes of ambulating</td>
<td>6 (29%)</td>
<td>1.5 (1, 3)</td>
</tr>
<tr>
<td>Episodes of neuro chair transfer (passive)</td>
<td>0</td>
<td>–</td>
</tr>
</tbody>
</table>

IR indicates interquartile range.
Comparison of patients rehospitalized for heart failure with versus without a history of habitual alcohol consumption

Ragesh Panikkath, MD, Natalia Suvorava, MD, Neena Ngo, Deepa Panikkath, MD, Sian Yik Lim, MD, Elvira Umyarova, MD, and Gary Meyerrose, MD

Alcohol paradoxically is known to have a protective and a deleterious effect on the heart. The effect of alcoholism on the growing problem of heart failure (HF) readmissions is not known. This study addressed this issue with a population of adult patients (>20 years old) who were re-admitted for HF within 30 days after a hospitalization for HF at a university hospital in West Texas for a period of 5 years. Of the 204 patients with HF who were readmitted, 130 were admitted for HF exacerbations and 74 for unrelated medical conditions. Seventy-two (55%) were men, and the patients’ mean age was 67 ± 15 years. Only 32 patients (24%) had a history of alcoholism. The mean age was significantly lower in patients with a history of alcoholism than in those without (62 ± 11 vs. 67 ± 15 years; P = 0.03), and there were more men in the group with a history of alcoholism (78% vs. 52%; P = 0.006). The mean ejection fraction was significantly lower in patients with a history of alcoholism than in those without (35 ± 19% vs. 39 ± 16%, P = 0.04). The length of stay was slightly longer in patients with a history of alcoholism, although the difference was not statistically significant (6 ± 5 vs. 5 ± 4 days; P = 0.52). Although alcohol contributed to only less than one quarter of hospital admissions, these patients were relatively younger and were predominantly males, compared to the sex-matched distribution of patients without a history of alcoholism.

Alcohol negatively affects several organ systems, including the cardiovascular system. Heavy alcoholism is known to be associated with alcoholic cardiomyopathy, which can increase the risk of ventricular arrhythmias and sudden cardiac death. However, alcohol is also known to have a cardioprotective effect, decreasing the risk for heart failure (HF) and death. Several studies have reported that moderate alcohol consumption is equal to abstinence in improving the ejection fraction (EF) of subjects who drink heavily and have alcoholic cardiomyopathy. Moderate alcohol consumption is also associated with a lower risk of HF in healthy individuals. The inverse risk of alcohol consumption was not mediated entirely through reduction of nonfatal myocardial infarction (MI) and was found even when adjusted for risk of MI in the Cardiovascular Health Study (1). Similarly, alcohol consumption in moderate amounts was associated with a reduction in MI in those with ischemic left ventricular (LV) dysfunction as well (2). Due to these contradictory reports regarding alcohol on the cardiovascular system, we studied the effect of alcohol on HF readmissions.

METHODS
This retrospective study comprised all adult patients (>20 years) readmitted with HF within 30 days of hospital discharge at a university hospital in West Texas. A detailed chart review of patients diagnosed with HF based on ICD-9 coding during the 5-year timeframe from January 1, 2007, to December 31, 2012, was done. The amount and type of alcohol consumed during this timeframe was recorded. One standard drink was defined as a drink containing 12 g of alcohol. Alcohol consumption in a week was categorized in four groups: nondrinkers (0 drinks), mild drinkers (1–6 drinks for men and 1–4 drinks for women), moderate drinking (7–21 for men, 5–14 for women), and heavy drinkers (>21 for men, >14 for women) based on the amount of alcohol consumed in a week. Data regarding alcoholism, illicit drug use, urine drug screen, LV size, EF, length of hospital stay, readmissions within 30 days, in-hospital complications, brain natriuretic peptide (BNP) values, and disposition status were collected. Patients who were admitted for reasons other than HF exacerbations were excluded from the study.

Pearson chi-square tests, Fischer’s exact tests, and independent samples t tests were used to compare the baseline characteristics, echocardiographic parameters, in-hospital complications, and disposition status. Patients who had a history of alcoholism were analyzed as a subgroup, and their characteristics were compared with characteristics of those who were readmitted with HF but without a history of alcoholism. All analyses were performed using SPSS Windows version 16.0. The study was approved by the institutional review board of Texas Tech University Health Sciences Center, Lubbock.

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RESULTS

Of the 204 patients with HF who were readmitted within 30 days of hospital discharge during the time period of the study, 130 were admitted for HF exacerbations. Of these 130 patients, 72 (55%) were men. The mean age of these patients was 67 ± 15 years. The mean time of hospital readmission was 14 days. Sixty-nine (53%) had diabetes, and 83 (64%) were hypertensive. Thirty-three (25%) had a history of implantable defibrillator implantation.

Of the 130 patients readmitted with HF, only 32 patients had a history of alcoholism (24%). Fourteen patients (11%) were drug abusers. The most common drug abused was cocaine in 12 patients. Quantitative BNP measurements were 10,290 ± 13,953 pg/mL. The mean EF was 38 ± 17%. Diastolic dysfunction was present in 49 patients (38%). The mean length of hospital stay during the readmission was 6 ± 4 days. In-hospital mortality was observed in 6 patients (5%), and five patients were referred to hospice care.

The characteristics were compared between patients with a history of alcoholism and those without (Table). The mean age was significantly lower in patients with a history of alcoholism than in those without (62 ± 11 vs. 67 ± 15 years; P = 0.03). Patients with a history of alcoholism were significantly more likely to be males (78% vs. 52%; P = 0.006) compared to a sex-matched population of patients without a history of alcoholism. Further, the mean EF was significantly lower in patients with a history of alcoholism than in those without (35 ± 19% vs. 39 ± 16%; P = 0.049). Two other values differed among those with a history of alcoholism, but the difference was not statistically significant: the mean BNP (8,214 ± 14,014 vs. 10,448 ± 14,264 pg/mL; P = 0.51) and the length of hospital stay (6 ± 5 vs. 5 ± 4 days; P = 0.52).

DISCUSSION

Alcoholic cardiomyopathy is classically associated with heavy intake of alcohol over prolonged periods of time. People quitting drinking may have improvement in EF in about 3 years. Although alcoholic cardiomyopathy is classically associated with systolic dysfunction, it is increasingly recognized that alcoholism can be associated with diastolic dysfunction as well. Diastolic dysfunction in the presence of a normal systolic function has been reported in one third of alcoholics. In our study, 38% of patients were found to have diastolic dysfunction. Alcoholic cardiomyopathy is more common in men, with women contributing to only 14% of cases. Corroborating this, in our study, patients who were readmitted with HF with a history of alcoholism were predominantly males.

Multiple studies such as the Physician Health Study I, Cardiovascular Health Study, and Framingham Study show that a moderate amount of alcohol consumption is associated with a lower risk of heart failure. This was true even among patients with severe LV systolic dysfunction in the SOLVD trial, where a lower risk of mortality was observed in people consuming alcohol in light or moderate amounts compared to nonalcoholics.

One possible mechanism of benefit is that alcohol consumption in moderate amounts could cause lowering of vascular resistance and thereby cause a reduction in blood pressure. Mild drinking can increase the levels of atrial natriuretic peptides and reduce the effects of norepinephrine and vasopressin.

Confounding factors might have influenced the studies reporting the beneficial effects of alcohol, although some studies tried to compensate for them. One confounding factor is the sick quitter effect, when patients quit drinking when they are sick (4). The healthy survivor effect is another confounder, where only the healthy drinkers survive to old age. Incorrect self-reporting of alcohol and the variations in temporal trends of alcohol consumption might also have confounded these studies. As reported in several studies, this study might also suffer from the limitations of alcohol self-reporting (5), temporal variations in alcohol intake over time, failure to include noncardiovascular morbidity and mortality related to alcohol, and differences in ethnicity and culture.

Table. Comparison of heart failure patients with and without a history of alcoholism

<table>
<thead>
<tr>
<th>Variable</th>
<th>History of alcohol consumption</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62 ± 11</td>
<td>67 ± 15</td>
</tr>
<tr>
<td>Men</td>
<td>78%</td>
<td>52%</td>
</tr>
<tr>
<td>Brain natriuretic peptide (pg/mL)</td>
<td>8,214 ± 14,014</td>
<td>10,448 ± 14,264</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>35 ± 19</td>
<td>39 ± 16</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>6 ± 5</td>
<td>5 ± 4</td>
</tr>
</tbody>
</table>

Antiphospholipid syndrome is an autoimmune disorder characterized by arterial or venous thrombosis, recurrent first-trimester pregnancy loss, and multiple additional clinical manifestations. We describe a man with severe atherosclerotic basilar artery stenosis and superimposed in situ thrombus who was found to have antiphospholipid syndrome.

CASE REPORT

A 44-year-old male heavy smoker presented to the emergency department following the acute onset of left-sided weakness while at work. The patient had no history of hypertension, hyperlipidemia, diabetes, or obesity. No personal or family history of deep venous thrombosis or hypercoagulable disorder was present. Noncontrast head computed tomography (CT) and CT angiography revealed severe distal basilar artery stenosis (Figure 1). Emergent intravenously administered tissue plasminogen activator (tPA) thrombolytic therapy provided brief improvement followed by worsening left-sided weakness. Digital subtraction angiography confirmed the CT angiography findings. Intraarterial tPA was administered into the region of severe atherosclerotic stenosis and presumed in situ thrombus approximately 3 hours after intravenous tPA with slight improvement in the size of the lumen and contrast flow. The following day, magnetic resonance imaging (MRI) revealed acute ischemic change within the rostral pons and midbrain (Figure 2).

Two days after admission, the patient’s neurologic status began to decline further, with interval loss of right upper and lower extremity motor function as well as severely dysarthric bulbar speech. Emergent repeat digital subtraction angiography with basilar artery endovascular stenting was performed (Figure 3). A hypercoagulability clinical evaluation revealed significantly elevated anticardiolipin antibodies (aCL) (IgG 31.9, IgM 66.2) and positive lupus-like anticoagulant. The patient received systemic anticoagulation with heparin followed by transition to warfarin. Aspirin was also initiated. The patient required tracheostomy and percutaneous gastrostomy. His right-sided weakness improved soon after stenting, and his dysarthric speech improved more gradually. The patient tolerated decannulation of his tracheostomy prior to discharge and was tolerating a dysphagia diet per speech therapy recommendations. He was discharged to a skilled nursing facility with a residual neurologic deficit of 4/5 right upper and lower extremity strength, 2/5 left upper extremity strength, and 0/5 left lower extremity strength.

DISCUSSION

Antiphospholipid syndrome (APS) is associated with persistently positive antiphospholipid antibodies (aPL), most commonly aCL and lupus-like anticoagulant (1). In the absence of an underlying connective tissue disorder, the syndrome is referred to as primary APS, while secondary APS is most commonly seen associated with systemic lupus erythematosus. Diverse neurological manifestations of APS include cerebrovascular disease (stroke, transient ischemic attack, and venous thrombosis) in addition to a multiple sclerosis–like syndrome, seizures, migraine headaches, and cognitive dysfunction (1, 2). These symptoms are thought to reflect manifestations of hypercoagulability-induced ischemia of neural tissue and possibly direct actions of aPL.

Experimental and clinical data have suggested an association of APS with atherosclerosis. Endothelial dysfunction, oxidative stress, platelet activation, and increased cell adhesion molecules are common to both diseases (3). Premature atherosclerosis may be the first clinical manifestation of APS, and in a case such as this where age-accelerated atherosclerosis is seen with superimposed thrombosis and subsequent rethrombosis, a hypercoagulable state such as APS should be considered. In a low-density lipoprotein receptor knock-out mouse model with aCL induced by immunization with human aCL from an APS patient, enhanced atherogenesis has been observed (3). Endothelial dysfunction has been demonstrated using positron emission tomography in patients with APS (3).

The treatment of patients with APS and thrombotic events is based on guidelines for venous thrombosis and ischemic
stroke. The Antiphospholipid Antibodies and Stroke Study showed no difference between aspirin therapy and warfarin; however, in patients with severe thrombotic central nervous system manifestations, long-term treatment with warfarin has been recommended (1). Statins may be beneficial in the reduction of aPL-induced endothelial cell activation and intracellular signaling (1, 2).

Basilar thrombosis is a neurologically devastating condition, with considerable mortality as well as frequently devastating neurologic outcomes to include the so-called “locked in” syndrome. Complete recanalization can be achieved in about 60% of patients. Survival rates in patients undergoing thrombolysis alone range from only 30% to 60% (4). Revascularization is strongly linked to improved clinical outcomes (5). Thrombolysis alone may be unable to achieve revascularization particularly in the setting of underlying atherosclerosis, and a residual high-grade stenosis may increase the risk of reocclusion (6). In the series reported by Shi et al, successful stent placement was achieved in 90% of patients following intraarterial thrombolysis (6). Stenting in the setting of APL has not been previously described.

Figure 1. (a) Coronal maximum intensity projection (MIP) reformatted image from the initial CT angiography demonstrates severe stenosis of the distal basilar artery (arrow). (b) Frontal and (c) lateral projections from the initial digital subtraction angiography following a right vertebral artery injection also reveal severe distal basilar artery stenosis (arrows).

Figure 2. (a) Axial diffusion trace image from the initial MRI demonstrates cytotoxic edema compatible with acute infarction within the left paramedian rostral pons (arrow). (b) Axial T2-weighted MR image demonstrates edema corresponding to the region of infarction (arrow). Note the absence of normal basilar artery flow–related signal loss compatible with slow flow or vascular occlusion (arrowhead).
Figure 3. (a) Lateral projection from the digital subtraction angiography (DSA) following a right vertebral artery injection reveals deployment of the stent within the distal basilar artery and resultant resolution of the stenosis. (b) A frontal projection from the postprocedural DSA shows correction of the stenosis. (c) Axial T2-weighted image following endovascular stenting demonstrates normal flow-related signal within the basilar artery (arrow). Evolving edema in the region of infarction is present (arrowhead).

Spinal cord ependymoma presenting with neurological deficits in the setting of trauma

Amin F. Saad, MD, Larry T. Nickell, MD, S. Sam Finn, MD, and Michael J. Opatowsky, MD, MBA

Ependymomas represent 4% of all primary central nervous system neoplasms in adults, with 30% occurring in the spinal cord. We describe a young man with neurological deficits following a motor vehicle accident who was found to have an intramedullary cervicothoracic ependymoma.

CASE REPORT

A previously healthy 18-year-old man presented to the emergency department following a motor vehicle accident. All four extremities were weak immediately following the accident, with right-sided weakness noted on initial physical examination. Head and cervical spine computed tomography (CT) revealed no abnormalities. Cervical spine magnetic resonance imaging (MRI) revealed an expansile intramedullary mass at the cervicothoracic junction (Figures 1a, 1b) and mild interspinous ligament sprain. The patient’s neurologic deficit resolved within 24 hours. The patient underwent laminectomy and laminoplasty with complete resection of the mass (Figure 1c) and had an uncomplicated postoperative course. Neurological examination immediately following surgery revealed decreased right lower extremity proprioception, 2+/5 strength at the right L2 to L3 levels, and 4/5 strength at the right L4 to S1 levels.

DISCUSSION

Ependymomas are the most common intramedullary neoplasm in adults and represent 60% of all intramedullary tumors. They arise from ependymal cells lining the central canal of the spinal cord. These tumors have a mean age of presentation of 38.8 years and a slight male predominance (57.4%) (1, 2). The clinical presentation of ependymoma is similar to that of other intramedullary lesions, with a prolonged history of slowly worsening myelopathic symptoms prior to diagnosis.

MRI evaluation is the imaging modality of choice in the patient with suspected cord neoplasm. Ependymomas are typically iso- to hypointense relative to the spinal cord on unenhanced T1-weighted images, with the vast majority exhibiting at least some degree of enhancement following intravenous gadolinium administration (1, 3, 4). T2-weighted images usually reveal a hyperintense intramedullary lesion. Ependymomas may cause hematomyelia as well as subarachnoid hemorrhage, with 20% to 33% of lesions displaying a “cap sign” of signal hypointensity at the lesion margins secondary to hemosiderin deposition from intralesional chronic microhemorrhages. Cysts are often associated with ependymomas, with the majority representing nontumoral (polar) cysts at the margins of the lesion. True tumoral cysts (surrounded by enhancement) arise less frequently (1, 3, 4).

The preferred treatment for spinal cord ependymomas is complete surgical resection. Current advances in microsurgical technique and intraoperative monitoring enable frequent complete resection without worsening postoperative neurologic function (5). In a series of 31 cases described by Chang et al (5), only 10% of cases were associated with worsening neurological function, while 26% showed improvement and the rest remained stable. The preoperative neurologic status of the patient is the greatest predictor of postoperative functional outcome (2, 5). Radiation therapy delays disease progression in patients treated with subtotal resection.


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Figure 1. MR images before and after resection. (a) Sagittal T2-weighted image reveals an expansile intramedullary mass (arrow) extending from the C7–T1 to the T2–T3 levels with rostral tumoral cyst formation (arrowhead). (b) Sagittal T1-weighted postgadolinium enhanced fat-saturated image demonstrates avid slightly heterogeneous enhancement of the mass (arrow). (c) Sagittal T1-weighted postgadolinium enhanced fat-saturated image following surgical resection reveals no evidence of residual enhancing tumor (arrow). A small amount of hemosiderin remains within the operative bed (arrowhead).

Avocations

CABG

The nurse flaunted full privilege of her license
And tasered light into my face
While sun was still stretching under the covers
And my mind flirted
With the daughter of the poppy
Dancing in my veins.

“It’s time for a walk,” she declared.
It was less than 12 hours since the bypass.
“It’s too early,” I muttered, shaking the cobwebs.
“Doctor’s orders.” And she started gathering
Host of wires and the tubes,
Annexed to my limbs and organs.

Propped up, I briefly stood
And promptly slumped to the floor.
The room turned a hybrid maze:
A Ferris wheel and a merry-go-round.
Tests revealed: machine and sponges had
Siphoned off half my blood.

And my intolerance of the opiate
Had my brain on a trampoline, but I felt no pain.
For two days I watched the room from the ceiling.
People came to shower wishes,
I have vague recollection.
If this is, they call high, I prefer the low.

—Amanullah Khan, MD, PhD

Dr. Khan (e-mail: aman1963@gmail.com) is an oncologist on the medical staff of Baylor Medical Center at McKinney. In addition to publishing over 100 research articles, he is an award-winning poet who has written poems in three languages.
**Ganglioglioma and migraine headache**

Amin F. Saad, MD, Kennith F. Layton, MD, MS, S. Sam Finn, MD, and Michael J. Opatowsky, MD, MBA

Mixed neuronal/glial neoplasms represent a minority of intracranial neoplasms, typically associated with a more favorable prognosis than the more common higher-grade glial neoplasms. We describe a young man with headache, confusion, and slurred speech who was found to have a ganglioglioma.

**CASE REPORT**

A 19-year-old man with a history of chronic migraine headaches beginning in his early teens experienced an acute sudden onset of severe headache without provocation. Until this point the patient’s headaches lacked atypical symptoms and responded well to over-the-counter medication, and thus he had not undergone previous imaging evaluation. His family noticed that he was confused and had slurred speech, a marked change in the typical character of his headaches. Upon presentation to the emergency department, a noncontrast brain computed tomography (CT) scan (Figure 1) revealed a 6.9 × 3.2 cm isodense nonhemorrhagic mass centered in the left occipital lobe with scattered coarse calcific deposits, surrounding vasogenic edema, and local mass effect but no midline shift or hydrocephalus. Subsequent magnetic resonance imaging (MRI) further characterized the extent of the mass and revealed conspicuous cystic components (Figure 2a). Mild heterogeneous enhancement was shown on the postgadolinium T1-weighted sequences (Figure 2b). On the MRI, calcific deposits appeared as hypointense foci on the susceptibility weighted sequence (Figure 2c). The patient underwent a craniotomy and the mass was resected. Histologic examination revealed findings compatible with a World Health Organization grade 1 ganglioglioma. The patient did well postoperatively without focal neurologic deficit and will follow up for routine surveillance imaging.

**DISCUSSION**

Gangliogliomas are an uncommon lesion, accounting for 0.4% to 0.9% of all intracranial neoplasms and 1% to 4% of pediatric central nervous system neoplasms (1). Despite being uncommon, they are the most common mixed neuronal-glial neoplasm (2). Gangliogliomas have a peak incidence in patients 10 to 20 years old, with 80% being found in individuals younger than 30 years. In a case series of 99 proven gangliogliomas, 38% occurred in the temporal lobe, 30% in the parietal lobe, and 18% in the frontal lobe (3). Provenzale et al presented a series of 25 gangliogliomas, including two occipital lobe lesions (8%). Gangliogliomas are the most common neoplastic etiology (40%) for chronic temporal lobe epilepsy, particularly partial complex seizures (1).

The imaging appearance of gangliogliomas is variable, with most presenting as mixed solid and cystic lesions (52%) (4, 5). A superficial cortical site of involvement is most commonly encountered (2, 5, 6). On CT, these lesions are most commonly hypoattenuating (38%), followed by mixed density (32%) and hyperattenuating (15%) (4). Calcific deposits most commonly occur in association with mixed solid/cystic masses and are seen in approximately 30% of gangliogliomas (2, 5). Based on CT appearance alone, calcified gangliogliomas may be indistinguishable from oligodendrogliomas.

The MRI appearance of gangliogliomas has classically been described as a cystic mass with an enhancing mural nodule (4, 5). The presence of enhancement, however, is not indicative of a higher-grade neoplasm. Provenzale et al described a trend toward increasing tumor volume and prevalence of cystic components in those gangliogliomas occurring in early childhood.
The preferred treatment for gangliogliomas is complete surgical resection. Adjuvant chemotherapy and radiation are typically reserved for malignant lesions, with gangliogliomas demonstrating a rate of malignant transformation as high as 6%. Optimal technical surgical resections usually result in the complete resolution of seizure activity with only rare tumor recurrences (7). Gangliogliomas and other mixed glioneuronal tumors may harbor BRAFV600E mutations, an area of potential targeted therapy with agents such as vemurafenib.


Figure 2. MR imaging. (a) Coronal T2-weighted image reveals a heterogeneous mass with prominent cystic components (arrow) centered within the left occipital lobe in the region of the calcarine fissure, with vasogenic edema extending to the posterior temporal and inferior parietal lobes. (b) Axial gadolinium enhanced T1-weighted image reveals moderate heterogeneous enhancement of the mass (arrow). (c) Axial susceptibility weighted image reveals punctate foci of diminished signal (arrow) compatible with calcific deposits seen on the noncontrast CT.
Intracranial hypertension and intracranial hypotension are on opposite ends of the intracranial pressure spectra. It is extremely uncommon for both to cause headache in the same patient in a span of several days. This report describes a young man with intracranial hypertension who developed a severe excruciating headache due to intracranial hypotension after a diagnostic lumbar puncture. It is paradoxical that lumbar puncture, which is supposed to be a treatment option for patients with idiopathic intracranial hypertension, leads to headache due to intracranial hypotension.

Intracranial hypertension and hypotension can cause headaches; however, it is uncommon for both to cause headache in the same patient since they are on the opposite ends of the intracranial pressure spectrum. We present a patient who had headache due to intracranial hypertension initially, but after spinal tap developed headache due to intracranial hypotension. This situation has been described in only four patients in the literature to our knowledge, all of whom had headaches due to idiopathic intracranial hypertension (IIH).

CASE DESCRIPTION

A 33-year-old man presented with headache and blurring of vision of 2 months’ duration. He had known obstructive sleep apnea, for which he had undergone multiple surgeries (tonsillectomy, adenoidectomy, uvulopalatopharyngoplasty). His body mass index was 30.5 kg/m² (height 1.82 m, weight 105 kg). A computed tomography (CT) scan of the head and magnetic resonance imaging (MRI) of the brain were normal. He had bilateral papilledema, worse on the left side than on the right. The cranial nerve and motor and sensory examinations were normal. Lumbar puncture showed elevated opening pressure (440 mm) of cerebrospinal fluid (CSF) (normal, 70–180 mm). Twelve mL of clear colorless fluid was drained for studies, which showed a normal protein, glucose, and cell count and no organisms (Gram stain or culture).

The patient’s headache improved temporarily but worsened later. The headache changed in character and was more positional. He felt worse when sitting up or walking and better in a lying-down position, making him bed bound for several days. An MRI with contrast showed pachymeningeal enhancement suggestive of headache due to intracranial hypotension (Figure 1). Conventional analgesics used for intracranial hypotension like caffeine and Excedrin failed to relieve his headache. An epidural blood patch utilizing 20 mL of autologous venous blood immediately relieved his headache. His pain medications were deescalated and he was discharged home the next day. A CT angiogram of the brain revealed chronic occlusion of the right sigmoid sinus collateralizing to an atretic right internal jugular vein (Figure 2). His vitamin A level was normal, and he was not on any medications known to cause intracranial hypertension.

DISCUSSION

The patient described developed headaches due to both intracranial hypertension and intracranial hypotension within a short span of time. There have been four case reports of a similar presentation in patients (three females and one male) who had headaches due to IIH.
The functions of CSF is to provide buoyancy to the brain. The intracranial hypotension is often less than 60 mm CSF. One of the mechanisms that could lead to headache due to intracranial hypotension is the postlumbar puncture headache. It is uncommon and paradoxical to have headache due to intracranial hypotension in patients with IIH for which the treatment of choice is drainage of CSF using a shunt.

The mechanism of causation of IIH is not clear; however, it could be due to an imbalance between CSF production and absorption. This is the basis of using procedures like lumboperitoneal shunts (thereby draining CSF and reducing intracranial pressure) in patients with severe symptoms due to IIH. On the other hand, the postlumbar puncture headache is due to pressure) in patients with severe symptoms due to IIH. The diagnosis of IIH is based on the modified Dandy criteria. IIH has a prevalence of 1 to 2 per 100,000 people and affects predominantly obese women of childbearing age (15–44 years) (1). More than 80% of patients with IIH are overweight women (2). Repeated lumbar punctures, thereby draining the CSF, have been used as a treatment option for this condition (3). One of the most common adverse effects of lumbar puncture is postlumbar puncture headache. It is uncommon and paradoxical to have headache due to intracranial hypotension in patients with IIH for which the treatment of choice is drainage of CSF using a shunt.

Since the cranium is a closed compartment, consisting of brain, blood, and CSF, an increase in the volume of any of these components can lead to headache. If the volume of the CSF is low, traction on the meninges can lead to pain as well. IIH is a heterogeneous syndrome characterized by increased intracranial pressure at rest without any apparent explanation. The diagnosis of IIH is based on the modified Dandy criteria. IIH has a prevalence of 1 to 2 per 100,000 people and affects predominantly obese women of childbearing age (15–44 years) (1). More than 80% of patients with IIH are overweight women (2). Repeated lumbar punctures, thereby draining the CSF, have been used as a treatment option for this condition (3). One of the most common adverse effects of lumbar puncture is postlumbar puncture headache. It is uncommon and paradoxical to have headache due to intracranial hypotension in patients with IIH for which the treatment of choice is drainage of CSF using a shunt.

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Cerebral venous sinus narrowing has been reported in up to 90% of patients with IIH in recent studies (1). Repeat studies after normalization of the intracranial pressure demonstrated normalization of this finding (1). The cerebral sinus narrowing might be a consequence of the increased intracranial pressure. However, venous sinus narrowing/thrombosis could cause increased intracranial pressure as well. This situation could represent the chicken or egg debate as to which occurs first. Our patient had features of chronic occlusion of the sigmoid sinus on the right side, which could have caused his intracranial hypertension; however, a chronic narrowing of his sinuses by IIH could have caused a secondary thrombosis in it as well. There is no clear answer to this question.

Analgesics and sumatriptan have been known to be ineffective in patients with headache due to intracranial hypotension. Caffeine is reported to be effective in this condition. An epidural blood patch is the treatment of choice for headache due to postlumbar puncture leak of CSF when conservative methods fail (5, 6). This treatment is believed to relieve the headache by closing the dural leaks in CSF. Displacement of CSF from the spinal canal as a result of the epidural blood patch has also been thought to be a mechanism of relief of headache due to CSF leaks. However, there is a concern that an epidural blood patch might lead to worsening of intracranial pressure (which can be symptomatic or asymptomatic), as reported in multiple case reports of patients with baseline intracranial hypotension/normal intracranial pressure (7).

In our patient, an epidural blood patch helped relieve his headache without rebound intracranial hypertension. Multiple mechanisms are proposed for causation of intracranial hypertension after epidural blood patch. Mokri et al reported that rebound increase in intracranial pressure could be due to either an increased CSF production in response to CSF fluid depletion or a disturbed mechanism of CSF resorption due to a prolonged leak of CSF (7). The closure of the leak in CSF leads to increased production without continuous CSF loss. The choroid plexus might adjust ultimately to this situation and gradually result in abatement of this condition. However, our patient tolerated this procedure well and did not have a headache after the procedure. He was discharged the next day, without analgesics.

The alien hand syndrome

Ragesh Panikkath, MD, Deepa Panikkath, MD, Deb Mojumder, MD, PhD, and Kenneth Nugent, MD

A 77-year-old woman presented with the complaint of observing her left hand moving without her knowledge while watching television. Her left hand stroked her face and hair as if somebody was controlling it. These movements lasted only half an hour but on recovery, she had left hemiparesis. Alien hand syndrome as the presentation of cardioembolic stroke is extremely rare but can be terrifying to patients.

Alien hand syndrome is a phenomenon in which one hand is not under control of the mind. The person loses control of the hand, and it acts as if it has a mind of its own. The etiology includes neurosurgery, tumor, aneurysms, and rarely stroke (1). This case is presented to create awareness of this interesting clinical scenario, which can be terrifying to the patients and confusing to the physicians who are not aware of it.

CASE DESCRIPTION

A 77-year-old woman with chronic atrial fibrillation had her anticoagulation stopped temporarily for spine surgery. No bridging with low-molecular-weight heparin was done. Two days later, while watching television, she noted her left hand flinging across her visual field. Her left hand stroked her face and hair without her will. She got terrified. Her attempts to control the left hand with the right hand were unsuccessful. She did not have any control of the left hand for almost 30 minutes as it continued to make purposeful movements. She later noted that her left upper limb was numb and slightly weak when she regained control. Her husband helped her to the car to take her to the hospital, and he noted that she was dragging her left leg while walking.

In the hospital, a computed tomography (CT) scan and magnetic resonance imaging (MRI) of the brain showed acute infarcts in both parietal lobes. Transthoracic and transesophageal echocardiograms did not show any evidence of thrombus. She gradually gained normal control of the left side over the next 6 hours. A diagnosis of stroke possibly due to cardioembolism was made. Her anticoagulation was resumed, and she was discharged home with advice to maintain anticoagulation at all times.

DISCUSSION

Alien hand syndrome, or Dr. Strangelove syndrome, is an interesting situation in which a person loses control of his or her hand, which starts to act independently. It describes involuntary complex goal-directed activity of one limb. Recent usage of the term “alien hand” is more liberal and requires having observable involuntary motor activity along with the feeling that the limb is foreign or that it has a will of its own (2). The syndrome has been reported after surgery on the corpus callosum and with brain tumors, aneurysms, degenerative diseases of the brain, and uncommonly stroke. Alien hand as a manifestation of cardioembolic stroke is extremely rare, with only a few cases reported in the literature.

Lesions implicated in causing alien hand syndrome include those in the corpus callosum and/or posterior parietal cortex, supplementary motor area, and the anterior cingulate cortex. Functional MRI has been used to study brain activity in patients with alien hand syndrome (3). In normal individuals, initiation of motor activity shows activation of multiple extensive neural networks. However, in patients with alien hand syndrome, only isolated activation of the contralateral primary motor cortex is observed (3). It has been proposed that lesions in the parietal cortex result in isolated activation of the contralateral primary motor cortex due to its release from the intentional planning systems. Damage to the parietal cortex can also cause lack of awareness of movements due to loss of proprioceptive feedback or left hemineglect (3). The combination of these factors results in initiation of spontaneous movements without the patient’s knowledge or will.

Alien hand syndrome has been reported to be associated with several abnormal involuntary movements when different regions of the brain, like the corpus callosum, parietal region, or frontal region, are involved. It can be classified into at least four categories: 1) diagnostic dyspraxia/intermanual conflict

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when one hand performs actions contrary to the other hand); 2) alien hand sign (a subjective feeling that the hand is not one's own); 3) syndrome of anarchic hand (when the affected hand performs goal-directed activity not under the will of the person); and 4) supernumerary hand (a feeling of having an extra limb) (4). Another type of alien hand is the levitating hand, where the affected limb tends to levitate without volitional action (4).

Alien hand might manifest as a self-groping behavior and self-oppositional behavior (5). Autocriticism has also been reported, with the person slapping the alien hand with the normal hand. The person loses control of the affected hand as if it is being controlled by an external force. The alien hand might grab onto things and the person might have to use the other limb to release the objects from it. At extremes, the alien hand has been reported to even suffocate the patient.

There is no established treatment for alien hand. It has been reported to last for several days to several years. Alien hand as a manifestation of cardioembolic transient ischemic attack has been reported only once based on our review (6). The extremely short duration of alien hand in this case report (30 minutes) is the shortest reported duration of this phenomenon recorded.

Pregnancy-associated systemic lupus erythematosus

Rahime Nida Ergin, MD

Systemic lupus erythematosus (SLE) is an autoimmune disease that classically manifests itself with fever, arthralgia, and rash, predominantly in women of childbearing age. The autoimmunity is against nuclear and cytoplasmic components; therefore, any organ system can be affected, and the clinical presentation spectrum is wide. Although rare, de novo SLE can be diagnosed in pregnancy. Herein, a woman who had SLE diagnosed in early pregnancy is reported. This and a previous report imply that SLE has diverse clinical presentations in pregnancy.

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease related to an insufficiency in the clearance of cellular materials after apoptosis (1–4). A recent study suggested that the higher chemokine/cytokine activity during pregnancy in SLE patients increases pregnancy-related complications and disease flares, despite a similar pattern of chemokine/cytokine fluctuations in healthy pregnant women (5). Pregnancy and SLE affect the immune system, increasing the risk of pregnancy-related complications such as abortions, stillbirths, prematurity, preeclampsia, and intrauterine growth retardation (6, 7). Antinuclear antibodies at low titers are more common in women with recurrent pregnancy loss (50%) than in controls (16%) (6). In a recent meta-analysis of pregnancy outcomes in patients with SLE and lupus nephritis, the maternal complications were determined as lupus flare (25.6%), hypertension (16.3%), nephritis (16.1%), preeclampsia (7.6%), and eclampsia (0.8%). The fetal complications were premature birth (39.4%), spontaneous abortion (16.0%), stillbirth (3.6%), neonatal deaths (2.5%), and intrauterine growth retardation (12.7%) (7). Patel et al reported two cases of de novo SLE in pregnancy (8). In this case presentation, we report another rare case of pregnancy-associated SLE diagnosed in early pregnancy, together with radiological examinations.

CASE PRESENTATION

A 30-year-old nulliparous white pregnant woman was admitted to the emergency department with complaints of dyspnea, palpitation, chest pain, severe abdominal pain, and tenderness. She was 6 weeks pregnant according to her last menstruation date and had a gestational sac consistent with that gestational week. She had no significant past medical history. Initial laboratory values are shown in Table 1. Within 2 hours of admission, her hematocrit, hemoglobin, and platelet values decreased significantly to 28%, 9.7 g/dL, and 189 × 10^9/L, respectively. Abdominopelvic ultrasonography revealed massive pelvic fluid, left pleural effusion (Figure 1), and an intrauterine sac, but the crown-to-rump length was not clearly seen. A diagnosis of acute abdomen was made, leading to an exploratory laparotomy to rule out a ruptured ovarian cyst or ectopic pregnancy. Laparotomy revealed neither an intraabdominal gynecological pathology nor a bleeding focus, except for 500 mL of serohemorrhagic fluid in the dependent portion of the pelvis. Due to an increased D-dimer value, subcutaneous enoxaparin 0.6 mg twice a day was started. Postoperative hematocrit values continued to decrease.

After the pregnancy was terminated with dilatation and curettage (D&C), detailed radiological evaluation of the thorax and abdomen with contrast-enhanced computed tomography revealed pericardial effusion, pleural effusion, and pelvic fluid (Figure 2). Liver function deteriorated further within the next 4 days. However, her hematocrit and hemoglobin values remained stable, while tachycardia and dyspepsia subsided after D&C. Bronchoscopy and hepatobiliary and portal Doppler ultrasonography are not described in the text.

**Table 1. Laboratory values of the patient on admission**

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
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<tbody>
<tr>
<td>Human chorionic gonadotropin β-subunit (mIU/mL)</td>
<td>13,000</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>10.9</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>31%</td>
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<tr>
<td>Platelet count (×10^9/L)</td>
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</tr>
<tr>
<td>Leukocyte count (×10^9/L)</td>
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</tr>
<tr>
<td>Alanine aminotransferase (U/L)</td>
<td>45</td>
</tr>
</tbody>
</table>

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showed no abnormalities. Ten days after the D&C, blood counts and biochemical values returned to almost normal levels. Serological workup showed positive antinuclear antibodies (1:1000 titer) and decreased levels of IgA (35 mg/dL) and C3 complement level (79 mg/dL). Tests for perinuclear and cytoplasmic antineutrophil cytoplasmic antibodies, anti-ds-DNA antibodies, interferon-gamma release assays for tuberculosis, herpes simplex virus IgM, Epstein-Barr virus IgM, and cytomegalovirus IgM were all negative. Familial Mediterranean fever was excluded by genetic testing. The patient was diagnosed with SLE and started on a regimen of colchicum dispersion tablet and Plaquenil 200 mg tablet twice daily. Under this medical treatment, all radiological findings and biochemical parameters returned to normal.

**DISCUSSION**

With its wide spectrum of clinical manifestations and health consequences, SLE further jeopardizes pregnancy in terms of fetal and maternal health (1–7). Though it is predominantly diagnosed in women of childbearing age, in a recent report de novo SLE in two pregnant cases was reported (8). One case was a 22-year-old black woman diagnosed at the sixth gestational week of her second pregnancy. Although her previous pregnancy was complicated by chorioamnionitis and preeclampsia, she did not develop SLE in that pregnancy (8). This might be due to some common genetic pathways in both SLE and preeclampsia regulating the complement system (9). The outcome was preterm rupture of membranes necessitating cesarean section with a preterm baby. The second case involved a 21-year-old nulliparous Caucasian woman diagnosed with SLE in the 11th gestational week. She developed severe SLE nephritis during pregnancy, necessitating hemodialysis with a poor pregnancy outcome. At the 26th gestational week she had a cesarean section due to uncontrolled hypertension. The baby died at the age of 9 months of respiratory failure. Interestingly, she was reported to have marked renal improvement after pregnancy (8).

Our patient was older than the previous reported patients and was diagnosed to have SLE in early pregnancy. However, the clinical presentations were different. In the previous report, the cases were rather stable and pregnancy could be maintained and followed up, but in our case, the patient was admitted to the emergency department with dyspnea, tachycardia, chest pain, abdominal pain, and tenderness and was found to have deteriorating hematocrit values and pelvic fluid on ultrasonography. Therefore, the pregnancy was terminated and an exploratory laparotomy was undertaken to rule out intraabdominal bleeding. These observations support that SLE has diverse clinical presentations even in pregnancy-associated cases. Pregnancy-associated SLE is diagnosed in early pregnancy and leads to poor pregnancy outcomes.

Multiorgan dysfunction related to chronic ketamine abuse

Joseph M. Pappachan, MD, Binu Raj, MBBS, Sebastian Thomas, MD, and Fahmy W. Hanna, MD

Ketamine abuse is being increasingly reported worldwide. The drug can produce a dissociative state and hallucinations, making ketamine a favorite recreational agent among drug addicts. Chronic ketamine abuse can damage many organs, including the brain, heart, liver, gastrointestinal tract, and genitourinary system. We report a patient with chronic ketamine abuse who presented with severe cachexia, upper gastrointestinal involvement, hepatobiliary dysfunction, and acute kidney injury.

CASE PRESENTATION

A 59-year-old man presented to the emergency department with vomiting, lower abdominal pain, dysuria, and urinary incontinence of 5 days duration. For several months he had a poor appetite and dyspepsia, and he had gradually lost weight. He was known to have chronic obstructive airway disease and enlarged kidneys detected by an ultrasonographic study. He had a 40 pack-year history of smoking, consumed about 20 units of alcohol (1 unit = 10 mL of pure alcohol) weekly, and inhaled ketamine powder intranasally almost every day for about 3 years. He lived alone and was not sexually active in the immediate past.

On examination he looked dehydrated and cachectic, and his sclerae were mildly icteric. His body mass index was 14.5 kg/m² and his blood pressure, 90/60 mm Hg. Biochemical and hematological laboratory results are shown in Table 1. The electrocardiograph and chest radiograph did not show any abnormalities. An abdominal ultrasonographic study revealed bilateral hydronephrosis and hydroureter, hypoechoic liver with periportal hyperechogenicity, and mild dilatation of the common bile duct. The urinary bladder wall was thickened with increased trabeculations. A computed tomographic scan of the abdomen without contrast revealed a full distended stomach (Figure 1a), bilateral hydronephrosis (Figure 1b) and hydroureter, and a thickened urinary bladder wall (Figure 1c). The bladder was contracted.

The patient was initially managed with intravenous hydration, thiamine, and continuous urinary drainage through an indwelling catheter. Esophagogastroduodenoscopy showed grade 3 esophagitis and mild gastritis. The histology from the esophageal mucosa revealed only chronic inflammatory changes. A magnetic resonance cholangiopancreatography showed mild dilatation of the proximal common bile duct with narrowing of the common hepatic duct without cholelithiasis. The cisterna chyli was also dilated. There was no evidence of intraabdominal malignancy. Screening tests for viruses (HIV, hepatitis A, B, C, E, Epstein-Barr virus, and cytomegalovirus), autoimmune liver disorders (autoimmune hepatitis, primary biliary cirrhosis, and primary sclerosing cholangitis), and metabolic liver diseases (hemochromatosis and Wilson’s disease) were negative.

The patient was further managed with oral and intravenous hydration, a multivitamin supplement, and omeprazole. The acute kidney injury and the liver function abnormalities improved gradually (Table 1). He gained 3 kg body weight within a week of inpatient medical treatment.

With a diagnosis of ketamine-induced multisystem illness, he was advised to refrain from further drug abuse and was discharged to a community-based drug rehabilitation program. His general health steadily improved, and on a subsequent outpatient clinic visit 2 months later, he weighed 50 kg (a total weight gain of 8 kg). An abdominal ultrasonographic study revealed complete resolution of the hepatobiliary abnormalities, the hydronephrosis, and the hydroureter on both sides.

DISCUSSION

Ketamine is a phencyclidine derivative that is licensed for anesthetic use in humans and in veterinary medicine, especially...
in developing countries. At higher doses, ketamine produces a dreamlike state, hallucinations, distorted visual perceptions, a sensation of a near-death experience, amnesia, and delirium, making it a favorite recreational agent of drug abuse (3). “Special K,” “Vitamin K,” “K,” “kit-kat,” “keets,” “super acid,” “super K,” “cat valiums,” and “jet” are the terms used by drug abusers for recreational ketamine. The usual illicit dose ranges from 50 to 100 mg (3, 4). Acute toxic effects of ketamine include tachycardia, abdominal pain, hypertension, raised intracranial pressure, muscle rigidity, cognitive dysfunction, and sometimes death (2, 5).

Urinary tract abnormalities are the most commonly reported chronic toxic effect related to ketamine abuse. With chronic use, the drug injures the urinary bladder, causing ulcers, cystitis, and fibrosis leading to urinary incontinence, hematuria, bladder overactivity and shrinkage, and, in the later stages, hydroureter and hydronephrosis (2, 6). The term “ketamine bladder syndrome” has been coined to describe this clinical entity. The smooth muscle relaxing property of ketamine was thought to be a pathogenic mechanism of urinary tract disease. Ketamine itself or its active metabolites were believed to cause injury to the urinary tract, although adulterants in the abused drug preparation were proposed as the cause by some authorities. Direct damage, microvascular injury, and immune mechanisms were thought to be the etiological factors (7). Recent evidence suggests that cytotoxic damage to the urinary tract by the drug is the cause for the abnormalities (8). By alteration of the epithelial cell-to-cell adhesion and cell coupling in the renal tract, ketamine causes damage through a nonclassical proinflammatory mechanism. Ketamine abuse more than three times weekly for more than 2 years has been found to be a significant risk factor for urinary tract disease (9). Although recovery is observed in most cases with an early intervention, irreversible damage may occur in chronic cases.

Cholestasis related to chronic ketamine abuse has been described recently (10, 11). The exact mechanism for cholestasis is not known. Biliary dyskinesia resulting from the direct effect of

Table 1. Biochemical and hematological laboratory data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reference value</th>
<th>Day after admission</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>130–170</td>
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</tr>
<tr>
<td>White cell count (10⁹/L)</td>
<td>4–11</td>
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</tr>
<tr>
<td>Absolute neutrophil count (10⁹/L)</td>
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<td>14.5</td>
</tr>
<tr>
<td>Absolute lymphocyte count (10⁹/L)</td>
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<td>1.2</td>
</tr>
<tr>
<td>Absolute eosinophil count (10⁹/L)</td>
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<td>0.0</td>
</tr>
<tr>
<td>Absolute monocyte count (10⁹/L)</td>
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</tr>
<tr>
<td>Platelet count (10⁹/L)</td>
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</tr>
<tr>
<td>Serum creatinine (mmol/L)</td>
<td>70–120</td>
<td>228</td>
</tr>
<tr>
<td>Estimated glomerular filtration rate (mL/min)</td>
<td>&gt;90</td>
<td>26</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>35–50</td>
<td>30</td>
</tr>
<tr>
<td>Globulin (g/L)</td>
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<td>20</td>
</tr>
<tr>
<td>Total bilirubin (μmol/L)</td>
<td>6–22</td>
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</tr>
<tr>
<td>Alkaline phosphatase (IU/L)</td>
<td>33–125</td>
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<tr>
<td>Gamma glutamyl transferase (IU/L)</td>
<td>8–64</td>
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<tr>
<td>Alanine transaminase (IU/L)</td>
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<td>46</td>
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<tr>
<td>Albumin corrected calcium (mmol/L)</td>
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<td>2.31</td>
</tr>
<tr>
<td>Inorganic phosphate (mmol/L)</td>
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<td>1.6</td>
</tr>
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<td>Magnesium (mmol/L)</td>
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<td>0.7</td>
</tr>
<tr>
<td>Thyrotropin (μU/mL)</td>
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</tr>
<tr>
<td>Free thyroxin (pmol/L)</td>
<td>9–19</td>
<td>17</td>
</tr>
</tbody>
</table>

Figure 1. A computed tomographic scan of the abdomen showing (a) a dilated and distended stomach with fluid level (arrow); (b) bilateral hydronephrosis (arrows); and (c) a contracted urinary bladder with a thickened wall (arrow).
the drug on the smooth muscles or through the vagus nerve may be the cause of cholestasis. Full recovery from the hepatobiliary disease over time has been observed with complete abstinence from ketamine abuse (10, 11).

Chronic abdominal pain is a common presenting complaint in ketamine abusers. The reported prevalence of upper gastrointestinal symptoms is up to 75% (2, 12). Gastritis has been demonstrated in 85% of those who had endoscopy (12). Complete relief of the symptoms is observed in most cases when patients abstain from the drug. Gastric dilatation and severe reflux esophagitis caused by chronic ketamine abuse has not been described in the medical literature previously. Ketamine has been shown to reduce the lower esophageal sphincter tone in nonhuman models (13). Smooth muscle relaxation in the upper gastrointestinal tract might have caused dysmotility, dilatation, and stasis of food in the stomach and chronic esophageal reflux in this patient. The severe cachexia mimicking malignant disease observed in our patient could have been related to upper gastrointestinal disease and the associated poor nutrition, although biliary dysfunction and acute kidney injury might have contributed to the pathogenesis.


Multiorgan dysfunction related to chronic ketamine abuse
High-intensity cardiac rehabilitation training of a firefighter after placement of an implantable cardioverter-defibrillator

Jenny Adams, PhD, Sandra DeJong, BSN, RN-BC, Justin K. Arnett, BS, Kathleen Kennedy, MS, Jay O. Franklin, MD, and Rafic F. Berbarie, MD

Firefighters who have received an implantable cardioverter-defibrillator (ICD) are asked to retire or are permanently placed on restricted duty because of concerns about their being incapacitated by an ICD shock during a fire emergency. We present the case of a 40-year-old firefighter who, after surviving sudden cardiac arrest and undergoing ICD implantation, sought to demonstrate his fitness for active duty by completing a high-intensity, occupation-specific cardiac rehabilitation training program. The report details the exercise training, ICD monitoring, and stress testing that he underwent. During the post-training treadmill stress test in firefighter turnout gear, the patient reached a functional capacity of 17 metabolic equivalents (METs), exceeding the 12-MET level required for his occupation. He had no ICD shock therapy or recurrent sustained arrhythmias during stress testing or at any time during his cardiac rehabilitation stay. By presenting this case, we hope to stimulate further discussion about firefighters who have an ICD, can meet the functional capacity requirements of their occupation, and want to return to work.

The National Fire Protection Agency (NFPA), which develops and promotes standards for firefighter health and safety, recommends that firefighters with an implantable cardioverter-defibrillator (ICD) retire or be permanently restricted from performing strenuous emergency duties (1). The cardiac rehabilitation (CR) program at Baylor Heart and Vascular Hospital in Dallas, Texas, was contacted by a firefighter from another state who, after ICD implantation, was put on restricted duty. Because he needed medical clearance to return to full active duty, he wanted to undergo the high-intensity, occupation-specific cardiac rehabilitation training program (HIOST) that we have developed for firefighters seeking to return to work after a cardiac event (2).

CASE REPORT

A 40-year-old off-duty firefighter with no significant past medical history suddenly collapsed after playing a game of racquetball. Friends retrieved and applied the automatic external defibrillator, which, after analyzing his cardiac rhythm, delivered a shock. When paramedics arrived, portable monitoring revealed ventricular fibrillation that necessitated a second shock; this initially restored a narrow-complex rhythm without the need for further intervention. The patient was transported to the hospital, where cardiac catheterization showed normal coronary arteries and an echocardiogram showed normal left ventricular systolic function without significant structural heart disease. He had no family history of heart disease or sudden cardiac death. He took no prescription medications, his physical examination was unremarkable, and his body mass index was 24 kg/m². Having survived an out-of-hospital cardiac arrest secondary to apparent idiopathic ventricular fibrillation, he underwent implantation of an ICD.

The patient attended six sessions of traditional CR in his hometown before transferring to the Baylor program in Dallas, where he consented to participate 3 days per week for a total of 18 HIST sessions. The training goal was to determine whether he could perform simulated firefighting tasks and exceed the required functional capacity of 12 metabolic equivalents (METs) (1) without his ICD delivering shock therapy.

During all 18 exercise training sessions, the patient’s ICD was evaluated before and after exercise. For the first 2 weeks, these device interrogations were done in person and consisted of a lead impedance test, an electrogram amplitude test or sensing test, and a capture threshold test. Thereafter, the ICD was interrogated using the manufacturer’s program designed for at-home defibrillator monitoring. The system allowed the patient to download all pertinent device information for remote evaluation. Under the supervision of an electrophysiologist, a clinical specialist (employed by the ICD manufacturer) reviewed each transmission for proper functioning of the device and for the presence of arrhythmias.

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At the beginning and the end of the 18-session series, the patient completed a treadmill stress test while wearing firefighter turnout gear and a calibrated portable metabolic system (K4b2, Cosmed USA Inc., Chicago, IL) that captured his oxygen consumption data (Figure 1a). The maximal stress test protocol included 2-minute stages at speeds of 3.3 to 4.2 mph and changes in grade from 0% to 25%. The indications for terminating the test were those designated by the American College of Sports Medicine (3).

The HIOST sessions were 75 minutes long and comprised different combinations of exercises to ensure that the patient’s training simulated the physical demands of firefighting. Nurses and exercise physiologists from the CR program provided exercise training, clinical testing, and monitoring during all sessions.

The HIOST workouts were customized by incrementally increasing not only the cardiovascular intensity but also the weight loads involved. While the patient trained, he wore a weighted vest that ranged from 10 to 55 pounds, the latter approximating the weight of his firefighter turnout gear. Some exercises, such as crawling under a barrier and using a stair-climbing machine, were for both muscular and cardiovascular endurance. Most of the simulated firefighting tasks involved carrying or using equipment, such as carrying a weighted box (range, 11.5 to 50 pounds), pulling a 30- or 60-pound fire hose, raising a pike pole weighing 5.5 to 15.4 pounds, hitting a tire for 20 to 60 seconds with a 9-pound sledgehammer, and climbing stairs while carrying a 15- or 30-pound hose (Figure 1b). Two exercises simulated victim rescue: 1) dragging a 50-, 95-, or 165-pound dummy along the ground, and 2) pulling a stair chair with a 50-pound dummy up two flights of stairs.

The high-intensity training was symptom limited, meaning that no heart rate or blood pressure limit was used to restrict exercise intensity. In conjunction with the device interrogation, the patient’s blood pressure was measured before and after exercise. His electrocardiogram was continuously monitored by telemetry, and peak heart rate and blood pressure measurements were recorded while he performed various training exercises. A physician was present in the rehabilitation room at all times.

During the HIOST sessions, the patient’s blood pressure and heart rate remained within acceptable ranges (means, 153/52 to 189/78 mm Hg and 182 to 196 beats/min, respectively). His mean peak rate-pressure product value (32,460 ± 3864) was consistent with the 36,000 threshold (4). One arrhythmia was noted: a single four-beat run of nonsustained ventricular tachycardia that was deemed clinically insignificant by the supervising cardiologist and the electrophysiologist who reviewed the case. The patient’s ICD never delivered shock therapy, and he had no adverse events or symptoms that required the discontinuation of any exercise session.

**DISCUSSION**

Firefighters with an ICD, such as the 40-year-old subject of this report, are asked to retire because they cannot fulfill NFPA essential job task 13: “Functioning as an integral component of a team, where sudden incapacitation of a member can result in mission failure or in risk of injury or death to civilians or other team members” (1). Concerns about sudden incapacitation are well founded, given that sudden cardiac death is the most common cause of on-duty fatalities among US firefighters (5, 6). A recent study of sudden cardiac death among firefighters aged ≤45 years identified the following risk factors: obesity, smoking history, left ventricular hypertrophy, coronary heart disease, and hypertension (7). The authors noted that obesity itself confers a twofold increased risk of sudden cardiac death, a finding that is especially worrisome in light of the high rates of obesity in the US fire service. Studies estimate that 30% to 40% of US firefighters are clinically obese; when the categories of overweight and obese are combined, the range is 73% to 88% (8). Our patient, who was forced to resign, was of normal weight and had none of the aforementioned risk factors for sudden cardiac death.

The US Department of Labor clearly outlines the job description of a firefighter (9). Many tasks are listed, some of which include strength activities defined as “very heavy work,” such as lifting, carrying, pushing, pulling, and climbing. In a study of the metabolic demands of simulated firefighting tasks, firefighters who were more fit completed the tasks (e.g., carrying a high-rise fire hose pack up three flights of stairs, advancing a fire hose, and performing a rescue and mannequin drag) faster than those who were less fit (10). The patient in this case had no limiting symptoms and received no ICD shock therapy while he performed similar tasks. Furthermore, he reached a functional capacity of 17 METs during a stress test, exceeding the 12-MET minimum required for his occupation.
We acknowledge that the patient has a risk of future ICD shocks and that we did not simulate an active firefighting environment during his CR. The likelihood of future shocks cannot be predicted, and it is impractical in a CR setting to reproduce the smoke, heat, and emotional stress of an actual fire scene. What we can do is simulate firefighting tasks as closely as possible during training and examine other ways of evaluating firefighters who want to return to work (e.g., stress testing them in turnout gear). Our goal in this case was to provide as much information as possible so the physicians involved could make a well-reasoned decision about the patient’s request for medical clearance.

To our knowledge, ours is the first report of a patient having an ICD placed for secondary prevention and then being able to exercise at a high functional capacity, with regular ICD interrogations showing no recurrent sustained arrhythmias. We present this case report to promote future discussion and clinical investigations about firefighters who undergo ICD implantation, are able to function at a high capacity, and want to return to active duty.

Acknowledgments

We thank the patient for allowing his story and photos to be published. We also thank the physicians of Texas Primary Care and the cardiac rehabilitation staff who approved and monitored his activity, and Beverly Peters, MA, ELS, who helped develop and prepare the manuscript.
Electrocardiogram in a 28-year-old woman with dyspnea on exertion

D. Luke Glancy, MD, and Fred A. Lopez, MD

A 28-year-old HIV-infected woman with dyspnea on exertion for 6 months had no history of acute rheumatic fever or opportunistic infections and no family history of heart disease. Her CD4 count 3 months earlier was 473/μL, and she was adherent with her antiretroviral therapy. On physical examination her neck veins were normal, as were her carotid pulses. The chest was clear to auscultation. A 1+/4+ left parasternal (right ventricular) lift was felt, and the left ventricular impulse was normal. The first heart sound was loud and split. The second heart sound was loud and palpable in the second left intercostal space. Heard at the cardiac apex were a soft pansystolic murmur of mitral regurgitation and an early low-medium pitched third heart sound immediately followed by a typical diastolic murmur of mitral stenosis. An electrocardiogram was normal except for signs of left atrial enlargement: a negative terminal portion of the P wave in lead V1 ≥ 0.1 mV in amplitude and ≥ 0.04 seconds in duration (2); P waves in leads II, III, aVF, V3, and V4 ≥ 0.12 seconds in duration (3); and bifid with >0.04 seconds between the 2 peaks (4) in leads III and V3 (Figure).

An echocardiogram explained how a patient with a third heart sound could have a typical murmur of mitral stenosis

From the Sections of Cardiology, Departments of Medicine, Louisiana State University Health Sciences Center and the Interim LSU Hospital, New Orleans, Louisiana.

Note: This patient, believed to be the first in the United States and the second in the world reported to have both HIV infection and atrial myxoma, was described in detail in the *Journal of the Louisiana State Medical Society* (1). The electrocardiogram, however, was neither illustrated nor described in detail in that report.

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**Figure.** Electrocardiogram in a 28-year-old woman with exertional dyspnea for 6 months. See text for explication.
by demonstrating a large left atrial myxoma that fell into the mitral orifice early in each diastole causing a “tumor plop” followed by a mitral stenosis murmur because the orifice of the valve was almost completely occluded. The mean diastolic pressure gradient across the mitral valve was 18 mm Hg as measured by echo-Doppler. Because the hemodynamics of left atrial myxoma and mitral stenosis are so similar, it is not surprising that both the physical exam and the electrocardiogram would be similar in the two conditions, with P waves suggesting left atrial enlargement being early electrocardiographic findings in both. The patient underwent uneventful operative removal of a $5 \times 4 \times 8.5$ cm left atrial myxoma.


Avocations

Spring at the Dallas Arboretum. Photo copyright © Rolando Solis, MD. Dr. Solis is an interventional cardiologist practicing at Baylor Medical Center at Garland and the Heart Hospital Baylor Plano (e-mail: rmsolis@me.com).
Fat in the ventricular septum

Erin E. Donaldson, DO, Jong Mi Ko, BA, Johannes J. Kuiper, MD, Themistokles Chamogeorgakis, MD, and William C. Roberts, MD

Described herein is a 68-year-old man who underwent cardiac transplantation for severe chronic heart failure resulting from ischemic cardiomyopathy. Examination of the excised heart showed not only extensive left ventricular scarring but also a huge collection of adipose tissue in the subepicardial region and surprisingly also in the ventricular septum. The finding of fat in the ventricular septum is extremely rare and prompted this report.

Fatty deposits in the heart, particularly in the Western world, are extremely common. The largest deposits occur in the subepicardial regions, particularly in areas adjacent to the coronary arteries; in the right ventricular and right atrial walls; in the atrial septum; less frequently in the left atrial wall; commonly in areas of scarring in the left ventricular free wall; and extremely rarely in the ventricular septum (1–3). The present report was prompted by finding considerable quantities of adipose tissue in the ventricular septum, apparently isolated from the subepicardial region.

CASE DESCRIPTION

A 68-year-old white man underwent cardiac transplantation because of severe heart failure resulting from previous myocardial infarcts, the consequence of atherosclerotic coronary heart disease. He apparently was in his usual health until age 36 when he had an acute myocardial infarction. At age 54 he underwent coronary artery bypass grafting, and at age 59 symptoms of heart failure appeared. At age 64 an intracardiac defibrillator was inserted, at age 66 atrial fibrillation appeared, and at age 67 a second myocardial infarct occurred. A left ventricular assist device was inserted not long thereafter. Exactly 12 months later, the cardiac transplant occurred.

The explanted heart “after cleaning” weighed 560 g. The left ventricular assist device weighed 350 g. The heart contained such large quantities of adipose tissue that it floated in a container of formaldehyde. (The patient’s body mass index was 28 kg/m².) All epicardial coronary arteries were severely narrowed by atherosclerotic plaque. Focal scars were present in the left ventricular free wall and ventricular septum, and isolated fatty deposits were present in the ventricular septum as well as in multiple other regions of the heart (Figure 1).

DISCUSSION

Described is a patient with extensive fatty infiltrates of the heart including a large deposit isolated to the ventricular septum. Such a finding has been described, to our knowledge, in only 3 previous reported patients. Spain and Cathcart (4) described a 59-year-old woman with complete heart block who at necropsy had “almost the entire myocardium [in the upper third of the ventricular septum] . . . replaced by fat.” No gross illustrations were provided. Nezafati and colleagues (5) described a 27-year-old woman who had a percutaneous biopsy of the right side of the ventricular septum because of a mass in the right ventricular outflow tract. Histologic examination disclosed “benign lipomatous hypertrophy.” Ak and associates (6) described a 54-year-old woman who by echocardiogram had a hyperechogenic mass in the ventricular septum protruding into the right ventricular outflow tract. The lobulated fatty structure arising in the ventricular septum was operatively excised. Histologic examination disclosed nonencapsulated adipose tissue. None of the 3 previously reported patients with ventricular septal fat had coronary arterial disease.

1. Roberts WC, Roberts JD. The floating heart or the heart too fat to sink: analysis of 55 necropsy patients. Am J Cardiol 1983;52(10):1286–1289.

From the Baylor Heart and Vascular Institute (Donaldson, Ko, Roberts) and the Departments of Internal Medicine, Division of Cardiology (Kuiper, Roberts), Pathology (Roberts), and Cardiothoracic Surgery (Chamogeorgakis), Baylor University Medical Center at Dallas. Dr. Donaldson is now with the Department of Family Medicine, Methodist Charlton Medical Center, Dallas, Texas.

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Figure 1. The heart in the patient described. (a) Cross-section of the right and left ventricles showing adipose tissue (yellow) in the ventricular septum and huge quantities of similar fat in the subepicardial region. Portions of the left ventricular free wall are scarred. (b) A close-up of the ventricular septum again showing the adipose tissue. (c) Another cross-section of the ventricles showing the adipose tissue in the ventricular septum totally surrounded by myocardium. (d) A close-up of the ventricular septal area.
We present an 89-year-old woman with newly diagnosed atrial flutter associated with a flare of her rheumatoid arthritis (RA). She had a history of diet-controlled type 2 diabetes mellitus, hypertension, and RA and presented with lightheadedness and worsening hand pain. She was found to be in new atrial flutter with rapid ventricular response and to have an active RA flare. In addition to adequate atrial flutter rate control, her RA flare was managed by adding hydroxychloroquine and doubling her existing methotrexate dose.

Atrial flutter is a common arrhythmia that carries a high burden of morbidity in the elderly population (1). Cardiac-specific mechanisms often are implicated in contributing to disease onset, but systemic factors may play an important role in triggering or initiating newly identified cases of atrial flutter.

CASE DESCRIPTION
An 89-year-old woman with diet-controlled type 2 diabetes mellitus, hypertension, and rheumatoid arthritis (RA) presented with lightheadedness and worsening hand pain. Her initial electrocardiogram revealed atrial flutter with variable block and a rapid ventricular response (Figure 1). Her body mass index was 31.2 kg/m², and her proximal interphalangeal joints were mildly warm and tender bilaterally (Figure 2). Her leukocyte count ranged from 10.4 to 14.6 × 10³/µL, and her erythrocyte sedimentation rate was 119 mm/h. Chest radiography and urine and blood cultures revealed no source of active infection, and she remained afebrile during the course of the admission. Her echocardiogram showed moderate left atrial dilation, mild right atrial dilation, thickened ventricular walls without wall motion abnormalities, and an ejection fraction of 65%. Her thyroid function testing was within normal limits. She had been admitted with acute kidney injury and mild altered mental status 2 weeks prior to the present admission. Due to concerns for potential medication-related side effects, her RA regimen was changed. Specifically, her hydroxychloroquine was discontinued and her methotrexate dose was decreased by half (from 20 to 10 mg/m² once weekly). No other medication changes to her home regimen preceded this admission.

During the current admission, her rapid ventricular response required high-dose multiagent nodal blockade to achieve adequate control. After several days of dose titration, her heart rate normalized with metoprolol succinate 150 mg twice daily, diltiazem sustained-release 180 mg twice daily, and digoxin 0.125 mg daily. She remained in atrial flutter throughout hospitalization, and her symptoms quickly resolved with heart rate control. Her RA flare was managed by reinstating the hydroxychloroquine and doubling the methotrexate dose to 20 mg weekly (her original dose).

DISCUSSION
Approximately 200,000 patients are newly diagnosed with atrial flutter annually in the United States (1). These estimates are likely higher in elderly patients with comorbid cardiopulmonary disease. In population-based studies, atrial flutter represents a predictor of late mortality independent of other traditional cardiovascular risk factors (2).

There is increasing recognition of the systemic inflammatory profile of RA and its potent effects on cardiac function. Mechanistically, RA may contribute to conduction disturbances (3) and progressive diastolic dysfunction (4). To the best of our knowledge, no data are available evaluating the association between RA and atrial flutter, and particularly RA flares and atrial flutter. Although often approached and managed similarly, atrial flutter and atrial fibrillation have distinct epidemiological and clinical risk factors (5). A Danish national cohort study of over 4 million patients in inpatient and outpatient care centers showed that patients with RA were at increased risk for atrial fibrillation and stroke, regardless of age and sex, over a mean follow-up of 4.8 years (6). A more recent investigation showed an increased rate of hospitalization for atrial fibrillation in RA patients compared with matched controls (7). However, after accounting for relevant baseline covariates, no increased risk of atrial fibrillation was observed.

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in RA patients (7). Our patient had evidence of a concurrent active RA flare given her exacerbated pain symptoms and elevated inflammatory markers. She developed atrial flutter after her RA medications were both discontinued and decreased, likely leading to an RA flare. Active disease and augmentation of circulating inflammatory markers may have contributed to her new-onset atrial flutter (8).

The implications of a potential relation between RA and atrial flutter are presently unclear. Routine screening of patients with systemic inflammatory disorders with electrocardiograms is controversial (9). Our initial experience raises the question of whether the relation between these clinical entities is coincidental, correlated, or causal. Our patient’s medical comorbidities and enlarged biatrial sizes likely increased her baseline risk of experiencing atrial flutter.


Figure 1. Presenting electrocardiogram that revealed new atrial flutter with variable block and rapid ventricular response.

Figure 2. Active inflammation of metacarpal and proximal interphalangeal joints in rheumatoid arthritis.
Adult T-cell leukemia/lymphoma is a rare malignancy associated with the human retrovirus human T-cell lymphotropic virus type 1. It is characterized by the proliferation of highly pleomorphic lymphocytes. Involvement of peripheral blood, bone marrow, lymph nodes, spleen, and extranodal sites such as skin, liver, gastrointestinal tract, and central nervous system can occur. There are four distinct clinical variants, and the prognosis and clinical course range from highly aggressive to a more protracted course depending on the subtype. We describe a man with de novo adult T-cell leukemia/lymphoma and discuss the unique clinical, morphologic, immunophenotypic, and molecular features of this entity.

A
dult T-cell leukemia/lymphoma (ATLL) is an uncommon lymphocytic malignancy associated with human T-cell lymphotropic virus type 1 (HTLV-1). This disorder is endemic in several regions of the world where HTLV-1 is prevalent, in particular southwestern Japan, the Caribbean basin, and parts of central Africa (1). The proliferation of highly pleomorphic lymphocytes with distinctive clinical, morphologic, and immunophenotypic features is characteristic (2). The diversity in clinical features and prognosis of this disease has led to its classification into four subtypes—acute, lymphomatous, chronic, and smoldering—which are defined by organ involvement, lactate dehydrogenase (LDH) levels, and calcium values (3). We report a case of de novo ATLL.

CASE PRESENTATION
A previously healthy 59-year-old Nigerian man presented with a 2-week history of a rapidly enlarging right-sided neck mass associated with dysphagia, odynophagia, and right neck pain. He had no weight loss, night sweats, or rash. Examination revealed a 10 × 6 cm firm conglomerate nodal mass in the right anterior cervical chain. Enlarged right supraclavicular lymph nodes, some enlarged left anterior cervical lymph nodes (1 × 1 cm), and right axillary adenopathy (3 × 2.5 cm) were also noted. A computed tomography (CT) scan of the neck revealed a 3.5 × 2.9 cm right palatine tonsillar mass with associated narrowing of the supraglottic larynx and oropharynx. The conglomerate nodal mass in the right side of the neck measured 10 cm in caudal dimension. There was obliteration of the right internal jugular vein and encasement of the right internal carotid artery. Further staging with CT of the chest, abdomen, and pelvis revealed massive subpectoral and right axillary adenopathy, with the largest subpectoral node measuring 4.8 × 2.7 cm. Several additional mesenteric nodes were noted, the largest of which measured 3.1 × 1.7 cm. There was splenomegaly of 12 cm. No bony lesions were seen on CT scan, and there was no evidence of hypercalcemia on presentation.

Notable laboratory values upon presentation included a white blood cell count of 20,000 K/μL, hemoglobin of 13.8 g/dL, and platelets of 204,000 K/μL. His LDH was 413 U/L (normal range, 0–250 U/L), and uric acid was 6.1 mg/dL. Results of an HIV test were negative. Review of the peripheral smear revealed numerous small- to medium-sized mononuclear cells with scant cytoplasm and convoluted nuclei, many of which had polylobated forms (Figure). Bone marrow aspirate also revealed many of the same mononuclear cells seen on the peripheral smear. Core biopsy and immunohistochemical stains showed a 60% cellular marrow with a small population of aberrant T cells with loss of CD7. Flow cytometry on the bone marrow revealed a 14% aberrant T-cell population expressing CD2, CD3 (dim), CD4, CD5, CD25, CD45, CD52, and CD123 (partial). These cells were negative for CD7 and CD8. Flow cytometry of peripheral blood revealed a 51% population of identical aberrant T cells. HTLV-1 antibody testing was positive by enzyme-linked immunosorbent assay and Western blot, confirming a diagnosis of ATLL, aggressive subtype.

Chemotherapy with cyclophosphamide, prednisone, doxorubicin, and vincristine (CHOP) in conjunction with zidovudine and interferon alpha was promptly initiated. After one cycle of chemotherapy, there was marked decline in the size of his adenopathy and corresponding improvement in his dysphagia, odynophagia, and neck pain. His course was complicated by Strongyloides stercoralis in the stool, which was treated with...
ivermectin. He also had neutropenic fever due to *Clostridium difficile* colitis, which resolved with oral vancomycin. A positron emission tomography (PET) scan performed after his third cycle of chemotherapy revealed no evidence of residual lymphoma, and allogeneic stem cell transplant was planned. He completed six cycles of CHOP chemotherapy in conjunction with interferon and zidovudine, but unfortunately there was evidence of diffuse osseous relapse on PET scan performed for restaging purposes prior to bone marrow transplant. This relapse was associated with bone pain and marked hypercalcemia, which was refractory to bisphosphonate therapy. Since his malignant T cells expressed CD52, second-line therapy with alemtuzumab was attempted, but he did not tolerate this therapy well and did not have a discernible clinical response. He was eventually transitioned to hospice and died shortly thereafter.

**DISCUSSION**

ATLL, a rare hematological malignancy, was first described in Japan in 1977 as a distinct, progressive T-cell leukemia with a peculiar morphology. Due to the clustering of the disease in the southwestern portion of Japan, a viral etiology was suspected (2). In the early 1980s, HTLV-1, the first human retrovirus discovered, was isolated from leukemic cells from a patient with ATLL. This finding of an association between HTLV-1 and ATLL led to the virus’s inclusion among human carcinogenic pathogens (4). Later, in the mid to late 1980s, HTLV-1 was found to be associated with other, primarily inflammatory, diseases including tropical spastic paraparesis, HTLV-1-associated myelopathy, HTLV-1 uveitis, and infective dermatitis (5). Around the same time, other endemic areas for the virus and its associated diseases were found in addition to southwestern Japan, including several Caribbean islands, tropical Africa, South America, the Middle East, and northern Oceania (6).

Approximately 20 million people worldwide are estimated to be infected with HTLV-1, and about 90% remain asymptomatic carriers throughout their lives. The cumulative risk of ATLL development among HTLV-1 carriers is estimated to be 2.5% to 5% over the course of a 70-year life span (7). Affected individuals are usually exposed to the virus early in life. Viral transmission predominantly occurs through breast milk, sexual intercourse, and exposure to peripheral blood and blood products (8). The disease has a long latency, and thus ATLL occurs only in adults with onset ages ranging from 20 to 80, with an average age of 58 years. Males are more commonly affected, with a male to female ratio of 1.5 to 1 (9).

Although HTLV-1 infection alone is not sufficient in and of itself to result in neoplastic transformation, the virus does express a few genes demonstrated to aid in oncogenesis (1). In HTLV-1–infected lymphocytes, the p40 tax viral protein has been shown to lead to transcriptional activation of many genes inducing proliferation and inhibiting apoptosis in vivo. Another gene recently described, the HTLV-1 basic leucine zipper factor (HBZ), which is uniformly expressed in ATLL cells, seems to have a more important role in cellular transformation and leukemogenesis than does p40 tax. HBZ transcription appears to be correlated with provirus load and also with the severity of disease (5). Nevertheless, additional undefined genetic alterations over time in addition to these appear to be required to result in malignancy.

Once malignant transformation does occur, patients with ATLL show a variety of clinical manifestations due to various complications of organ involvement by leukemic cells, opportunistic infections, and/or hypercalcemia. These three factors often contribute to the extremely high mortality of the disease (1). Most patients present with widespread lymph node involvement as well as involvement of peripheral blood. The distribution of the disease is usually systemic, involving the spleen, extranodal sites including the skin and liver, and less common sites such as the lung, gastrointestinal tract, and central nervous system (10). The number of circulating neoplastic cells does not correlate with the degree of bone marrow involvement, suggesting that circulating cells are recruited from other organs such as the skin. In fact, the skin is the most frequent extralymphatic site, with involvement in more than 50% of cases. Large nodules,
plaques, ulcers, and erythrodermas are observed (11). Immune suppression is common at presentation and during the course of disease progression. In a nationwide study in Japan, approximately 26% of 854 patients with ATLL had active infections at diagnosis. The infections were bacterial in 43%, fungal in 31%, protozoal in 18%, and viral in 8% of patients (12).

The diagnosis of ATLL requires the detection of characteristic cells in peripheral blood or tissue samples. Typical ATLL cells have convoluted nuclei with homogeneous and condensed chromatin, small or absent nucleoli, and agranular, basophilic cytoplasm. In the peripheral blood, the polylobated appearance of neoplastic cells has led to the term “flower cells,” which are considered characteristic of ATLL (13). ATLL cells in the skin and lymph node can vary in size from small to large, with forms including pleomorphic to anaplastic to Hodgkin-like with no specific histological pattern of involvement. The differential diagnosis includes Sézary syndrome, other peripheral T-cell lymphomas, and Hodgkin lymphoma, and establishing the true diagnosis can at times be difficult without demonstration of the presence of HTLV-1 (1).

After the diagnosis of ATLL has been established, determination of its subtype—which reflects prognostic factors, clinical features, and the natural history of the disease based on the presence of organ involvement, leukemic manifestation, and values for LDH and calcium—is necessary for the selection of appropriate treatment. The four subtypes have been identified as acute, lymphomatous, chronic, and smoldering ATLL (3). The acute variant is the most common and is characterized by a leukemic phase, often with a markedly elevated white blood cell count, skin rash, and generalized lymphadenopathy. This systemic disease is accompanied by hepatosplenomegaly, constitutional symptoms, and elevated LDH. Hypercalcemia, with or without lytic bone lesions, occurs in 50% of patients with the acute variant. Parathyroid hormone-related protein or receptor activator of nuclear factor kappa B ligand (RANKL) produced by ATLL cells is considered the main cause for hypercalcemia. Many patients with the acute variant also have an associated T-cell immunodeficiency, which frequently leads to opportunistic infections such as Pneumocystis jirovecii pneumonia and strongyloidiasis, the latter of which was present in our patient (14). The lymphomatous variant is characterized by prominent lymphadenopathy, which is similar to the acute form but differs in that there is no peripheral blood involvement. Most patients present with advanced stage disease, although hypercalcemia is seen less often, in about 17% of cases.

In the less aggressive chronic and smoldering forms, symptoms are nonspecific and there is no tumor mass or lymphadenopathy. While an absolute lymphocytosis may be present in the chronic form, atypical lymphocytes are not numerous in the peripheral blood. The smoldering variant differs from the chronic variant in that the smoldering type is associated with a normal white blood cell count but with >5% circulating neoplastic cells (3). Mild lymphadenopathy and hepatosplenomegaly may be present in the chronic form, but these manifestations are not present in the smoldering form. Hypercalcemia does not occur in either the chronic or smoldering subtypes. Cutaneous lesions can be seen in all four subtypes. Progression from the chronic or smoldering to the acute variant occurs in 25% of the cases, but usually after a long duration (1). The survival rate varies depending on the subtype, with 4 to 6 months for the acute type, 9 to 10 months for the lymphomatous type, 17 to 24 months for the chronic type, and 34 months to >5 years for the smoldering type (14).

Immunophenotypically, tumor cells characteristically express pan T-cell antigens CD2, CD3, and CD5 but usually lack CD7. Prototypical ATLL cells have a CD4+, CD8+ mature helper T-cell phenotype, although a few cases are CD4+, CD8+ or double positive for CD4 and CD8. CD25 is strongly expressed in nearly all cases, and malignant cells frequently also express the chemokine receptors CCR4 and FOXP3, features of regulatory T cells (15). The large transformed cells may be positive for CD30, but anaplastic lymphoma kinase and cytotoxic molecules are negative, which helps to distinguish this entity from anaplastic large cell lymphoma (16). Although cytogenetic studies do not show specific recurrent abnormalities, almost all ATLL cases have a high degree of numerical and structural chromosome abnormalities, and molecular studies always demonstrate T-cell receptor genes to be clonally rearranged (17). Neoplastic cells show monoclonal integration of HTLV-1, while clonal integration is not present in healthy carriers (18).

ATLL can range from indolent to very aggressive, and treatment strategies are usually offered to patients with acute, lymphomatous, and unfavorable chronic variants while patients with typical chronic and smoldering ATLL are observed initially. Although chemotherapy is warranted, ATLL has been shown to be resistant to most regimens, and enrollment in clinical trials is recommended if possible. The monoclonal antibody alemtuzumab (anti-CD52) has also shown some efficacy, but responses are still transient and further disease progression is inevitable (19). Although autologous hematopoietic cell transplantations do not appear to be of benefit due to frequent early relapses, allogeneic cell transplantations offer a potential graft-versus-leukemia effect and may be considered for patients with an available donor (20).


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**Avocations**

A Gentoo penguin and chicks. Photo copyright © Jed Rosenthal, MD. Dr. Rosenthal is a cardiologist in Dallas, Texas (e-mail: jedr2@sbcglobal.net).
Malignant rhabdoid tumors (MRT) of the kidney are rare in children and even less common in adults, with only six previously reported adult cases. We present the case of a 60-year-old man with an MRT arising in the left kidney with extensive pulmonary micrometastases and thromboembolism resulting in thrombotic pulmonary microangiopathy (pulmonary tumor embolism syndrome). MRT is an extremely aggressive neoplasm with a short survival time.

Malignant rhabdoid tumor (MRT) of the kidney is a highly aggressive, extremely rare neoplasm that is usually seen in children. The term rhabdoid is used because the tumor cells resemble rhabdomyoblasts but lack myogenic markers, and pathologic diagnosis requires familiarity with these microscopic features plus awareness that adult onset is possible. We describe clinical and necropsy findings in an adult with primary renal MRT.

CLINICAL HISTORY

A 60-year-old white man with known hypothyroidism, hypertension, and chronic obstructive pulmonary disease had progressive fatigue and abdominal distension for 6 months and worsening dyspnea for 2 weeks. Imaging showed bilateral pulmonary infiltrates consistent with pneumonia, and he was treated at home with antibiotics and prednisone. Three days later, he presented to an outside emergency department with gross hematuria, hemoptysis, painful testicular swelling, and nontraumatic ecchymoses. He was then transferred to Baylor University Medical Center at Dallas and admitted to the intensive care unit. Examination disclosed bilateral lower-extremity edema and ecchymosis over the left calf and ankle. His body mass index was 30.4 kg/m², blood pressure, 170/90 mm Hg; heart rate, 96 beats/minute; respiratory rate, 18 breaths/minute; white blood cell count, 31.9 k/μL; hemoglobin, 9.3 g/dL; hematocrit, 25.9%; platelets, 81 k/μL; prothrombin time, 18.0 seconds (reference range 9.0–12.0 seconds); blood urea nitrogen, 46.0 mg/dL; creatinine, 1.6 mg/dL; and arterial blood gas pH, 7.38. He was given heparin and multiple units of red blood cells and cryoprecipitate. Chest radiograph showed bilateral basilar and right upper lobe infiltrates. Computed tomography showed a thrombus within the left renal vein that extended into the inferior vena cava and a mass in the mid to lower pole of the left kidney (Figure 1).

Over the next few days, the patient’s oxygen requirements increased, his abdomen became more distended, and his urine output decreased. A left radical nephrectomy and retroperitoneal lymph node dissection was performed. At surgery, there was no residual thrombus in the left main renal vein. Postoperatively,
he continued to bleed and developed an abdominal compartment syndrome; the same day at reoperation a splenectomy was performed for apparent “decapsulation,” and he died on the operating table.

The left kidney (surgical specimen) contained a $3.5 \times 2.5 \times 2.0$ cm poorly circumscribed, soft tan lesion in the mid to lower pole that extended from the hilum to the cortex. Numerous tan-gray nodules (0.1–0.4 cm) were also present within perinephric and renal sinus connective tissues. Microscopically, this MRT contained characteristic sheets of anaplastic, noncohesive tumor cells with eccentric nuclei, prominent nucleoli, and eosinophilic, fibrillar cytoplasmic inclusions (Figure 2). There was extensive intravascular tumor within adjacent soft tissues. Immunohistochemically, tumor cells were strongly reactive for vimentin and pancytokeratin (AE 1–3), but negative for desmin, myoglobin, S100, melanoma cocktail, TTF-1, CK7, CK20, CDX2, PAX8, CD31, CD34, Factor VIII, CD30, and CD45. Additionally, tumor cells were negative for integrase interactor 1 (INI-1) nuclear protein expression. Electron microscopy found cytoplasmic whorls of intermediate filaments, some of which displaced the nucleus (Figure 3). Together, these histologic, immunohistochemical, and electron microscopic findings were sufficient for the diagnosis of MRT.

At necropsy, the abdomen contained 90 g of clotted blood at the nephrectomy site. Subcentimeter grey-white tumor nodules were present in pulmonary hilar lymph nodes, the left adrenal gland, the left spermatic cord, and the right kidney. The inferior vena cava contained loose fragments of thrombus, and there were large, coiled thromboemboli in bilateral hilar lung vessels. Microscopically, all tumors had the same histologic appearance. The large pulmonary thromboemboli were laminated, and most contained tumor cells. In some sections, the tumor cells extended along endothelial surfaces of the pulmonary arteries, and small, intravascular fibrin thrombi containing tumor cells were widely distributed throughout both lungs (Figure 4). Additional autopsy findings included severe pulmonary emphysema, pulmonary hypertensive vasculopathy, chronic thyroiditis, and chronic gastroesophageal inflammation.

DISCUSSION

MRT of the kidney usually affects children <2 years of age (1). It comprised 1.8% of all pediatric renal tumors in the National Wilms’ Tumor Study (2). In 1978, MRT of the kidney was described as a “rhabdomyosarcomatoid variant of Wilms tumor” by Beckwith and Palmer because the cells resembled...
rhabdomyoblasts (3), but further studies failed to demonstrate myogenic differentiation (1), and eventually MRT was recognized as a distinct clinicopathologic entity (4). These tumors have also been reported to arise in the urinary bladder, gastrointestinal tract, mediastinum, liver, soft tissue, orbit, uterus, and central nervous system (5, 6), and MRT may be “pure” or associated with other malignant patterns (as “composite” tumors) (1).

Adult renal MRT is even less common, and only six cases have been reported (1, 7–11). Age at diagnosis has ranged from 32 to 60 years with no predominant gender. One patient was Asian, one was Caucasian-Hispanic (Spanish), and the remaining four were Caucasian non-Hispanic; all patients presented with symptoms related to the renal mass or to lung metastases. The postdiagnosis survival time was usually only a few months (1). Histologically, all tumors contained noncohesive cells with eccentric vesicular nuclei, prominent nucleoli, and fibrillar, eosinophilic cytoplasmic inclusions.

MRT is immunohistochemically perplexing because of frequent dual reactivity for vimentin, a mesenchymal marker, and cytokeratin, an epithelial marker (12); this dichotomy raises interesting questions regarding the origin of these unusual tumors. Chromosome 22q11.2 deletions or mutations eventually led to the discovery of INI-1 as the tumor suppressor gene mutation involved in renal and extrarenal MRTs (13), and these studies have firmly established MRT as a distinct entity (14). Furthermore, one fascinating hypothesis is that there is no single cell of origin for MRT, and that diverse cell types (even tumor cells) may give rise to an MRT as a consequence of acquired or congenital mutations involving the INI-1 gene.

Criteria essential for pathologic diagnosis of MRT include characteristic histology showing rhabdoid features (as described above) and immunohistochemistry indicating loss of INI-1 protein nuclear expression. Although not essential for diagnosis, negative myogenic markers and electron microscopic confirmation of cytoplasmic intermediate filaments in swirls or whorls provide additional support for this diagnosis. Also, loss of INI-1 is helpful to differentiate MRT from other primary renal neoplasms (15) with rhabdoid differentiation including clear cell, transitional cell, papillary, chromophobe, and collecting duct carcinomas (16–18).

Intravascular coagulopathy associated with a pulmonary tumor embolism syndrome also contributed to this patient’s death. Pulmonary thrombotic microangiopathy is uncommon, reported in only 3% to 26% of autopsied patients with solid tumors (19–22), and is usually only diagnosed postmortem (23). In this condition, embolic tumor cells obstruct pulmonary vessels, activate the coagulation cascade (24), and produce inflammatory mediators promoting thrombosis and intimal proliferation (23). This disorder results in increased vascular resistance, secondary pulmonary hypertension (24, 25), and right-sided heart failure. Such patients generally have widely disseminated cancer, and their prognosis is dismal.


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Spontaneous complete remission of angioimmunoblastic T-cell lymphoma

Michael S. Humeniuk, MD, Jackson J. Liang, DO, Matthew Howard, MD, and David J. Inwards, MD

Angioimmunoblastic T-cell lymphoma (AITL) is a rare hematologic neoplasm that typically presents with B symptoms, anemia, and lymphadenopathy. Its overall prognosis is poor, with a 5-year survival rate of 30%. We present a case of AITL that went into spontaneous remission, an uncommon occurrence.

CASE REPORT

A 63-year-old man with a congenitally bicuspid aortic valve and benign prostate hypertrophy presented to the emergency department complaining of cyclical fevers and 20-pound unintentional weight loss over the previous 3 weeks and was admitted to the hospital for workup of fever of unknown origin. These fevers reached 40°C and occurred regularly at 6- to 12-hour intervals, lasting 90 minutes each time before resolving completely. Review of systems was also positive for urinary retention, frequency, and perineal burning sensation.

The patient had spent large amounts of time in many countries in Africa, Eastern Asia, and South and Central America. While in Egypt 2 years earlier, he was bitten by a spider and developed significant left cervical lymphadenopathy. A cervical lymph node biopsy in Poland was reportedly benign. The procedure was complicated by left spinal accessory nerve damage, and 6 months prior to onset of his presenting symptoms he underwent surgical repair of the nerve at our institution. At that time another cervical lymph node was biopsied, which was benign, and his lactate dehydrogenase (LDH) level was 183 U/L (normal, 122–222 U/L).

Physical examination revealed bilateral tender cervical and submandibular lymphadenopathy, but no axillary or inguinal lymphadenopathy. A harsh precordial systolic murmur consistent with aortic stenosis was audible. No hepatosplenomegaly was found. Except for the presence of IgG antibodies to Epstein-Barr virus (EBV) viral capsid antigen and Epstein-Barr nuclear antigen, serologic testing for multiple infections was negative (Table 1). Results of a peripheral smear, blood cultures, and urinalysis were all negative, and the chest x-ray showed no infiltrates. Computed tomography scan of the abdomen revealed periaortic and periportal lymphadenopathy and splenomegaly. Flow cytometry revealed no increase in aberrant CD3/CD16-positive T cells or increase in natural killer cells. T-cell receptor gene rearrangement showed clonal T cells. Due to the clinical presentation and elevated inflammatory markers (Table 2), he was diagnosed with acute prostatitis. Ciprofloxacin led to prompt resolution of fevers. He was discharged home on day 5 with antibiotics but returned within a week due to fever recurrence. At this time, magnetic resonance imaging of the prostate...
ruled out prostatic abscess. Echocardiogram showed no sign of endocarditis, but revealed bicuspid aortic valve stenosis. He was continued on antibiotics for presumed persistent prostatitis.

Two weeks after this second discharge he was hospitalized again due to recurrent fevers and urinary symptoms. He now had progressive anemia and splenomegaly palpable to 2 cm below the costal margin. Biopsies of a hypervascular cervical lymph node revealed an atypical lymphoid infiltrate with clonal T-cell receptor gene rearrangements suspicious for T-cell lymphoma versus reactive paracortical T-cell hyperplasia. A positron emission tomography–computed tomography (PET-CT) scan (Figure 1a) revealed significant fluorodeoxyglucose (FDG)-avid splenomegaly and lymphadenopathy both above and below the diaphragm, worrisome for lymphoma.

Bone marrow biopsy revealed an atypical T-cell infiltrate suggestive of peripheral T-cell lymphoma, with no cytogenetic abnormalities. Subsequently, excisional biopsy of two FDG-avid cervical lymph nodes confirmed a diagnosis of AITL with patchy EBV uptake (Figure 2). He was discharged on oral ciprofloxacin for outpatient follow-up.

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Figure 1. PET-CT scan before and after remission. (a) Initial scan showing splenomegaly and diffuse lymphadenopathy. (b) Restaging scan demonstrating complete remission.

Table 2. Laboratory values from first hospitalization for fever (month 0) to month 10.5

Spontaneous complete remission of angioimmunoblastic T-cell lymphoma

July 2014
His fevers improved and due to the clinical improvement, he sought out a second opinion on his diagnosis at a second large academic cancer center. This center confirmed that the clinical picture and histopathological specimen were most consistent with AITL and recommended a chemotherapy regimen of cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) and vorinostat. Prior to initiation of chemotherapy, he underwent successful aortic valve replacement with a bioprosthesis and two-vessel coronary artery bypass grafting.

At his hematology follow-up 3 weeks after cardiac surgery, he was asymptomatic and denied recurrence of fevers, night sweats, and lymphadenopathy. Prechemotherapy PET-CT (Figure 1b) was performed, which showed no evidence of FDG-avid lymphadenopathy, suggesting complete spontaneous remission. He had received no therapy (including corticosteroids)

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**Figure 2.** Excisional lymph node biopsy. (a) Hematoxylin and eosin staining of the excisional lymph node biopsy shows effacement of the lymph node by a paracortical infiltrate of small to intermediately sized lymphocytes with irregular nuclear contours (40× and 400×). Immunohistochemical staining (100×) demonstrates an infiltrate of (b) CD3-positive T cells which coexpress (c) CD4 and (f) CD279, and a small subset of which coexpress CD10 (not pictured). (d) Reactive CD8-positive T cells are interspersed. (e) CD20-positive B cells are displaced to the periphery of the node. Chromogenic in situ hybridization of Epstein Barr virus–encoded RNA shows patches of positive B cells.
between the two PET-CT scans and thus he was not started on chemotherapy.

He returned for follow-up 6 months later and a repeat PET was performed, which showed no FDG-avid lymph nodes but did show increased marrow FDG avidity with elevated LDH. A bone marrow biopsy showed atypical lymphocytes and persistently decreased hematopoiesis but no signs of lymphoma. Two weeks later without any therapy, the LDH declined to 235 U/L and continued to decline. From this point forward he had no further lymphoma recurrence. For his hypoproliferative anemia, he was started on transfusions and prednisone therapy. He responded well and after 1 month was no longer transfusion dependent. Prednisone was subsequently tapered from 80 mg daily and discontinued 3 months later. At outpatient follow-up 12 months after being off corticosteroids, his lymphoma remained in remission.

**DISCUSSION**

AITL is a rare hematologic disease that classically presents with lymphadenopathy, hepatosplenomegaly, hypergammaglobulinemia, anemia, and B-type symptoms and is distinguished by distinctive lymph node architecture disruption. AITL subjects typically present with the previously mentioned symptoms and have a mostly nondiagnostic workup until a full lymph node excision is performed. The lymph node biopsies show effacement of the lymph node architecture. Bone marrow or other lymphoid organ biopsies can be abnormal but typically show a nonspecific polymorphic inflammatory infiltrate (1). Although the disease was thought to be possibly premalignant when first discovered, there are clonal T cells present (2), and research has been directed to identify the origin of these cells. The majority of cells are typically CD4 positive, but there does seem to be an overproduction of follicular helper T cells, showing CD10 positivity, PD-1 (CD279) positivity (3), and often Bcl-6 positivity (4), which are thought to be the likely precursor cells. Supporting this view is the finding of increased amounts of CXCL13, which is produced by follicular helper T cells for helping B cells migrate to germinal centers in and around the abnormal cells (5). Analysis also shows the presence of EBV-positive B cells, but the significance of EBV infection in the setting of AITL remains unclear. The presence of the EBV-positive B cells, which were present in our patient, may be a result of acquired immunodeficiency from the malignancy or a consequence of unregulated T and B cell interaction, with the proliferation of the abnormal B cells being merely a bystander phenomenon (2). The disease has a relatively poor prognosis, with an overall survival at 5 years of 30% to 35% and a median survival of 36 months (2). Currently used regimens include CHOP (and rituximab plus CHOP as the role of B-cell proliferation is still uncertain in the disease process) (6) and cyclophosphamide, vincristine, and prednisone. Since it is a T-cell malignancy, the use of cyclosporine has been introduced as a potential therapy (7). In a retrospective study, 8 of 12 subjects responded to therapy, with 3 having a complete response. Another new therapy is alemtuzumab, a monoclonal antibody to CD52 expressed by most of the T cells in this disease (8). Interestingly in this disease, most subjects die from overwhelming infection rather than direct lymphoma progression. This has led many to believe that this disease causes an acquired immunodeficiency that has yet to be elucidated (2). Our subject had most of the typical features at initial presentation, with anemia, lymphadenopathy, hepatosplenomegaly, B symptoms, and elevated LDH. Although some of the initial B symptoms could have been related to prostatitis, the subsequent anemia and fevers after antibiotics were more likely the direct result of the lymphoma and would have eventually led to his diagnosis.

The spontaneous remission of AITL without therapy is quite unusual and, although not unknown to the medical literature (9–11), is still a very rare occurrence. Little is known regarding predictors of spontaneous remission; however, one study showed factors that might predict this event (11). It showed that having an extra third chromosome was associated with a higher chance of spontaneous remission (P = 0.02) and an extra X chromosome showed an insignificant trend for less chance of remission (P = 0.09). Our patient did not have extra chromosomes. Careful surveillance following spontaneous remission is necessary, as many in the literature subsequently relapsed.

Myeloid sarcoma as the presenting symptom of chronic myelogenous leukemia blast crisis

Rebecca A. Levy, MD, Mabel A. Mardones, MD, Micah M. Burch, MD, and John R. Krause, MD

Myeloid sarcoma is an extramedullary tumor composed of immature myeloid cells that efface the underlying tissue architecture. It is usually associated with acute myelogenous leukemia, but can be associated with myeloproliferative neoplasms, myelodysplastic disorders, or myeloproliferative/myelodysplastic syndromes. If it is unrecognized, appropriate chemotherapy may be delayed and survival jeopardized. We present a case of a myeloid sarcoma presenting in an otherwise asymptomatic patient who ultimately was found to have chronic myelogenous leukemia, presenting in blast crisis. We also review the distinct clinical and pathologic features of myeloid sarcoma, as well as treatment of the disease.

Previous nomenclature for myeloid sarcoma included granulocytic sarcoma, myeloblastoma, extramedullary myeloid tumor, and chloroma. The term chloroma is derived from the Greek chloros, meaning green, as the tumor appears green when exposed to air (1). Myeloid sarcoma is associated with a small percentage of acute myelogenous leukemia (AML) cases, approximately 3% to 5% (2). However, myeloid sarcomas can also arise in the setting of chronic myelogenous leukemia (CML) in blast crisis. The pathologic diagnosis of myeloid sarcoma can be challenging on hematoxylin and eosin sections alone. Immunohistochemical stains help to characterize the cell of origin and provide definitive diagnosis of myeloid sarcoma. Once diagnosed, myeloid sarcoma is treated according to the associated underlying disease state.

CASE PRESENTATION

A 35-year-old previously healthy man presented with right posterior shoulder pain. A firm, fixed 2 cm soft tissue mass was palpated in the region of the right scapula. In addition, a nontender 4 cm axillary lymph node was palpated. Imaging with computed tomography of the chest revealed a single lytic lesion within the inferior angle of the right scapula. The differential diagnosis included metastatic disease, infection, and lymphoma. A core needle biopsy was performed of the right axillary node, and histologic evaluation revealed a monotonous population of medium-sized cells with vesicular chromatin and small nucleoli with a background of eosinophils and scattered megakaryocytes (Figure 1). The immature mononuclear cells stained positive for progenitor markers (CD34 and CD117) and myeloperoxidase.

The morphologic and immunophenotypic findings supported the diagnosis of myeloid sarcoma.

Subsequently, a bone marrow aspirate and biopsy were performed. Review of the peripheral blood revealed moderate leukocytosis (18.3 k/μL) with an absolute neutrophilia, left shifted myeloid lineage, and rare (2%) circulating blasts. The bone marrow biopsy was 90% cellular with markedly increased reticulin fibrosis (grade 3 of 3). Immunohistochemical stains on the bone marrow biopsy showed 15% to 20% CD34-positive blasts (Figure 2). Fluorescence in situ hybridization was positive for the BCR/ABL1 gene rearrangement in 84% of interphase cells. Chromosome analysis identified the presence of the Philadelphia chromosome [t(9;22)] in 17 out of 20 cells. Molecular studies were positive for the t(9;22) BCR/ABL1 major (p210) fusion transcript in 63.85% International Scale (IS) by reverse transcriptase–polymerase chain reaction (RT-PCR) quantification analysis. These findings were diagnostic of the blast phase of CML with fibrosis.

The patient was treated with dasatinib 140 mg daily for 2.5 months and referred for allogeneic stem cell transplant. A repeat bone marrow was performed after 2 months of dasatinib treatment. The aspirate smear showed 2% blasts with a myeloid to erythroid precursor ratio of 1:1. The aspirate clot displayed 80% cellularity with trilineage maturation. Flow cytometry found no increase in myeloblasts. There was no morphologic evidence of residual disease. However, molecular studies were positive for the t(9;22) BCR/ABL1 major (p210) fusion transcript in 1.04% IS by RT-PCR quantification analysis. Fluorescence in situ hybridization was positive for the BCR/ABL1 gene rearrangement in 4% of interphase cells identified. These findings signified a complete hematologic response and partial cytogenetic response at 2 months. Approximately 4 months after his diagnosis, the patient received an allogeneic matched unrelated donor transplant.
DISCUSSION

In our patient, the initial presentation of a soft tissue myeloid sarcoma led to the diagnosis of an underlying CML in blast crisis. Although asymptomatic, the underlying reticulin fibrosis suggested the disease had been present in a chronic phase for some time. The diagnosis of CML in blast crisis may not have been made or may have been further delayed if not for the detection of the myeloid sarcoma in this otherwise asymptomatic patient.

Review of prior publications revealed a high misdiagnosis rate of myeloid sarcoma. It is most frequently misdiagnosed as non-Hodgkin lymphoma, but can also be mistaken for Ewing sarcoma/primitive neuroectodermal tumor and undifferentiated carcinoma (3, 4). When based solely on hematoxylin and eosin stain, the diagnosis is incorrect in approximately 50% of cases (5). Furthermore, given the poor median survivals and options for long-term remission or cure in CML blast crisis, prompt and accurate diagnosis of this disease is imperative.

When considering the diagnosis of myeloid sarcoma, an appropriate panel of stains includes several immunohistochemical stains and special stains, specifically CD34, CD43, lysozyme, myeloperoxidase, CD68 (monocyte marker), CD163 (monocyte marker), and CD117 (3, 4, 6). It can be helpful to include a CD3 and CD20 stain to exclude non-Hodgkin lymphoma. The most sensitive markers for myeloid sarcoma are CD43, lysozyme, myeloperoxidase, and CD68 (4). Myeloperoxidase is localized to the primary granules of myeloid cells and occurs early in differentiation, making it a helpful marker for identifying myeloid lineage. No single immunohistochemical stain can establish the diagnosis of myeloid sarcoma; rather, a combination of morphologic findings and several immunohistochemical and special stains are required.

CML is a myeloproliferative disease characterized by the presence of the BCR/ABL1 fusion gene. The CML chronic phase classically presents with neutrophilic leukocytosis with an increased percentage of myelocytes, metamyelocytes, bands, and segmented neutrophils (7). There is also frequently an

Figure 1. Right axillary node biopsy. (a) Low-power image (hematoxylin and eosin, ×100) and (b) high-power image (hematoxylin and eosin, ×400) of immature cells and dyspoietic megakaryocytes. (c) CD34 by immunohistochemical stain highlights the blasts within the myeloid sarcoma (immunohistochemical stain, ×400). (d) CD163 (a monocyte/macrophage marker) is positive in background histiocytes, which are brown stellate staining cells (immunohistochemical stain, ×400).
absolute basophilia in CML. The bone marrow is hypercellular with a dense layer of paratrabecular immature granulocytes and <5% blasts. Reticulin fibrosis can be identified in 30% of cases in the initial marrow, which is associated with a worse prognosis (8).

CML blast phase can be diagnosed if the blast count is at least 20% of the white blood cells in the peripheral blood or in the nucleated cells in the bone marrow. It can also be diagnosed if an extramedullary blast proliferation is identified (i.e., myeloid sarcoma). Prior studies have reported a range of 7% to 17% prevalence of extramedullary disease in patients with CML blast phase (9–11). In most cases, the blast proliferation is of myeloid origin, and a minority of cases display a lymphoid proliferation (12). Immunophenotypic analysis by flow cytometry and/or immunohistochemical stains can help differentiate the blast origin. Extramedullary blast proliferations are commonly identified as myeloid sarcomas and most commonly present in lymph nodes, soft tissue, skin, and bone (3); however, they have been documented in many other organs.

Blast crisis remains a challenge in the management of CML. The introduction of BCR-ABL tyrosine kinase inhibitors has fundamentally changed the natural history, prognosis, and treatment of CML. Survival in chronic-phase CML is now estimated at a median of 25 to 30 years (13). As such, progress to blast crisis has been reduced to approximately 1% per year compared to 20% per year in the pre-imatinib era (13, 14). However, median survival after diagnosis of blast crisis currently ranges from 7 to 11 months compared with 3 to 4 months in the pre-imatinib era, which illustrates a less-than-desirable improvement (15–17).

Once blast crisis has been diagnosed, management depends on previous therapy and type of leukemia (myeloid or lymphoid) (13, 15). Best results are achieved for the few patients who return to chronic phase and are successfully transplanted (14). Available choices for newly diagnosed, tyrosine kinase inhibitor–naïve patients include imatinib, dasatinib, or nilotinib (15–17). Also, the recent approval of next-generation tyrosine kinase inhibitors like bosutinib and
ponatinib provides clinicians multiple treatment options for patients with advanced-phase CML (18). Appropriate patients should be referred early for allogeneic stem cell transplant. Even in the imatinib era, the best outcomes continue to be observed for patients who undergo allogeneic stem cell transplant. According to the German CML Study Group, the 3-year survival of 28 imatinib-pretreated patients transplanted in advanced phases (25 in blast crisis) was 59% (14, 17). Current guidelines recommend considering allogeneic stem cell transplantation after a reasonable attempt has been made with a suitable tyrosine kinase inhibitor—selected therapy according to the mutation profile (15). If tyrosine kinase inhibitors alone are not sufficient, acute leukemia-type induction therapy should be pursued. Therefore, the best management of blast crisis is its prevention by an early and rigorous reduction to low levels or elimination of BCR-ABL (13).

The advent of tyrosine kinase inhibitor therapy has tremendously improved the clinical outlook for patients with CML. However, the number of effective treatment options is limited in advanced-phase (accelerated phase or blast crisis) CML, and treatment modalities effective in chronic-phase CML are not nearly as effective in advanced-phase CML (18). Active clinical research of investigational agents and combination regimens is needed to expand treatment options available to patients such as the one presented here.

Acute lymphocytic leukemia with superimposed invasive aspergillosis and pneumopericardium successfully treated with voriconazole

Carlos L. Alviar, MD, Bryan Doherty, MD, and Muthiah Vaduganathan, MD, MPH

We present a 47-year-old man with acute lymphocytic leukemia with a pericardial friction rub heralding pericardial aspergillosis. The clinical course was complicated by pneumopericardium, likely secondary to a direct connection between the lung parenchyma and the pericardial space. Bronchoalveolar lavage cultures returned positive for methicillin-resistant *Staphylococcus aureus* and *Aspergillus niger*. Combination voriconazole and vancomycin resulted in symptomatic improvement within 2 weeks of hospitalization.

Aspergillus pericarditis is a rare clinical entity but is associated with potentially life-threatening complications that pose significant medical and surgical challenges to effective management (1–5). This case describes a case of Aspergillus pericarditis in a patient with leukemia.

**CASE DESCRIPTION**

A 47-year-old white man with acute lymphocytic leukemia (ALL) who had completed chemotherapy (Linker regimen) presented to the oncology clinic with mild left-sided pleuritic chest pain of a week’s duration, associated with anorexia, occasional minimal hemoptysis, and shortness of breath with exertion. His course of chemotherapy was discontinued 3 weeks earlier due to neutropenic fever of unknown origin, which was treated empirically with vancomycin and piperacillin/tazobactam with subsequent resolution of symptoms. The patient’s social history was notable for active smoking (45 pack-years total) with prior alcohol and intravenous drug use. He was cachectic-appearing and tachypneic, but hemodynamically stable. Diffuse fine crackles were audible at both lung bases, and a prominent pericardial rub was detected throughout the precordium and was accentuated during systole. No Kussmaul’s sign or pulsus paradoxus was evident. He had a stable hemoglobin of 8.9 mg/dL, a serum sodium of 128 mEq/dL, and an albumin of 1.6 g/dL. Serial troponin and creatine kinase (total and MB fraction) measurements were negative. The chest x-ray revealed bilateral perihilar infiltrates suggestive of an infectious process. The electrocardiogram revealed concave ST segment elevation in V3 and V4 of 4.5 mm with concomitant PR segment depression. A transthoracic echocardiogram revealed a moderate-sized circumferential pericardial effusion that was not hemodynamically significant. A computed tomography (CT) image of the chest showed bilateral pulmonary cavities with a “halo formation” concerning for a necrotizing fungal pneumonia. The CT also showed that one of the cavities was in direct contact with the pericardium, creating a communication between the pulmonary parenchyma and the pericardial space (Figure). Blood cultures remained negative throughout the hospital course. A bronchoscopy revealed necrotizing pneumonia, which was neutrophil predominant and had concomitant vascular involvement. Cultures from the bronchoalveolar lavage isolated methicillin-resistant *Staphylococcus aureus* and *Aspergillus niger*.

Cardiothoracic surgery elected not to perform pericardial biopsy or undertake more invasive evaluation in this high-risk patient given his poor baseline functional status and his significant underlying comorbidities. The patient was started on amphotericin B, which was ultimately transitioned to voriconazole. Combination voriconazole and vancomycin was continued and resulted in symptomatic improvement within 2 weeks of hospital admission. The patient was discharged home in stable clinical condition on oral voriconazole for a total antifungal course of 12 weeks.

**DISCUSSION**

This report describes an unusual case of invasive aspergillosis presenting as fungal pericarditis in a patient with baseline immunosuppression complicated by pneumopericardium. To date, only 36 other cases of Aspergillus pericarditis have been reported since 1955. Among these, Aspergillus-related pericarditis was diagnosed before death in 13 of 36 patients, all of whom had established premortem diagnoses of invasive aspergillosis at other sites and had received antifungal therapy. *A. fumigatus* was the most common species, isolated in 28 cases (77%). *A. niger*, the species identified in our case, was found in only 4 cases (11%). In postmortem series, less than 5% of all patients

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with invasive aspergillosis had evidence of pericardial infiltration (6–8). This condition occurs primarily in severely immuno-compromised patients and is generally a result of contiguous dissemination of Aspergillus from the lung or myocardium (9, 10). Aspergillus inoculation into the pericardium after invasive cardiac surgery has been previously documented (11). Leukemia was the most common predisposing condition, with a frequency of 47% (17 cases) (9).

The introduction of air into the pericardial space secondary to a fungal infection is extremely rare. The Table summarizes the five known cases (including the present report) of invasive aspergillosis complicated by pneumopericardium (2–5). All cases involved men with prior histories of leukemia, with similar clinical presentations of chest pain and dyspnea. Based on the CT findings, a necrotizing pulmonary parenchymal process likely promoted the formation of a direct communication with the airway system. Only one other case had identified A. niger in the pericardial fluid (3).

The prognosis of patients infected with Aspergillus with pericardial involvement is generally very poor (2, 4). Despite the increased morbidity and mortality, treatment regimens are similar to those for other forms of invasive aspergillosis. All other previous cases of Aspergillus-associated pneumopericardium were treated with conventional amphotericin B therapy with mixed outcomes and prolonged hospital courses (2–5). Based on the limited available data, however, voriconazole appears to have superior pericardial penetration compared with other agents, and current treatment guidelines favor this agent in the treatment of invasive aspergillosis (12–15). Medical management with voriconazole in our case resulted in early symptomatic recovery in a high-risk cachectic patient.

Table. Summary of reported patients (all men) with leukemia, invasive aspergillosis, and pneumopericardium

<table>
<thead>
<tr>
<th>First author</th>
<th>Year of study</th>
<th>Age (years)</th>
<th>Type of leukemia</th>
<th>ECG ST elevation</th>
<th>Drug Rx</th>
<th>SD</th>
<th>Duration of Rx prior to recovery (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Müller (2)</td>
<td>1987</td>
<td>40</td>
<td>CML</td>
<td>N/A</td>
<td>A</td>
<td>+</td>
<td>N/A</td>
</tr>
<tr>
<td>Owens (3)</td>
<td>1990</td>
<td>14</td>
<td>ALL</td>
<td>+</td>
<td>A</td>
<td>+</td>
<td>8</td>
</tr>
<tr>
<td>van Ede (4)</td>
<td>1994</td>
<td>29</td>
<td>AML</td>
<td>+</td>
<td>A+I</td>
<td>–</td>
<td>N/A</td>
</tr>
<tr>
<td>Merino (5)</td>
<td>1995</td>
<td>7</td>
<td>ALL</td>
<td>N/A</td>
<td>A+I</td>
<td>–</td>
<td>4</td>
</tr>
<tr>
<td>Alviar</td>
<td>2014</td>
<td>47</td>
<td>ALL</td>
<td>+</td>
<td>A+V</td>
<td>–</td>
<td>2</td>
</tr>
</tbody>
</table>

+, indicates present; –, absent; N/A, not available or applicable; A, amphotericin; ALL, acute lymphocytic leukemia; AML, acute myelogenous leukemia; CML, chronic myelogenous leukemia; ECG, electrocardiogram; I, itraconazole; Rx, treatment; SD, surgical decompression; V, voriconazole.


Clinical and morphologic findings in disseminated *Scedosporium apiospermum* infections in immunocompromised patients

Molly M. Campa-Thompson, MD, James A. West, MD, Joseph M. Guileyardo, MD, Cedric W. Spak, MD, MPH, Louis M. Sloan, MD, and Stacy G. Beal, MD

*Scedosporium apiospermum* is a ubiquitous, saprophytic, filamentous mold that may cause localized, subcutaneous infections in immunocompetent hosts, but disseminated infection in severely immunocompromised patients. This mold is often highly resistant to multiple commonly used antifungal drugs. Even with treatment, there is a high mortality rate. We present two patients with fatal disseminated *S. apiospermum* infections after bone marrow and lung transplantation. This infection can be rapidly fatal, and survival may be improved by early recognition.

*Scedosporium apiospermum* (teleomorph state, *Pseudallescheria apiospermum*) is a ubiquitous, saprophytic, filamentous mold. It is found in the environment, including in soil, sewage, polluted water, and compost (1, 2). It cannot be transmitted from person to person (3). Immunocompetent patients can acquire subcutaneous infections (mycetoma), but disseminated infection is possible in patients with severely immunocompromised states, such as hematopoietic or solid organ transplant recipients. *Scedosporium* spp. account for approximately 25% of non-*Aspergillus* mold infections in transplant patients (1). Histologically, this organism is indistinguishable from *Aspergillus, Fusarium*, and many other molds, with septate hyphae branching at 45-degree angles. Therefore, identification requires culture from the infected organ (2). It is a highly resistant organism, with a notable innate resistance to amphotericin B and variable susceptibility to other antifungals (2). In this paper, we present the clinical and autopsy findings of two patients with fatal disseminated *S. apiospermum* infection.

CASE REPORTS

Case 1

A 72-year-old man with a history of myelodysplastic syndrome and transformation to acute myelogenous leukemia received a bone marrow transplant from a human leukocyte antigen–matched unrelated donor. Sixty-one days after his bone marrow transplant, the patient was noted to have decreased mental status. A head computed tomography (CT) scan with contrast revealed the development a 2.6 cm ring-enhancing lesion within the posterior aspect of the right frontal lobe that had mild surrounding vasogenic edema and local mass effect—findings that are typical for a pyogenic abscess (Figure 1a). The patient was also noted to have multiple black raised skin lesions, which were biopsied and cultured to yield the diagnosis of fungal infection by *S. apiospermum*. This was concordant with positive blood cultures done at the same time. The patient was treated with voriconazole and micafungin, and immunosuppressive drug doses were reduced. Despite intervention, the patient continued to decline and had radiologic evidence of progression of disease (Figure 1b, 1c). Eventually the patient instituted a do-not-resuscitate order and was placed on end-of-life care. He died 73 days post–bone marrow transplant.

Relevant autopsy findings included multiple necrotic abscesses within the myocardium and multiple areas of softening and red-brown discoloration within the brain parenchyma (Figure 2a). Microscopic examination showed a dense fungal infiltrate. The fungus displayed 45-degree angle, dichotomous branching and septate hyaline hyphae (Figure 3a). Microscopically, there were hyphae in sections of the brain abscesses as well as in the leptomeninges, liver, and lung. Postmortem blood cultures were positive for *S. apiospermum*.

Case 2

A 62-year-old man with a history of atrial fibrillation and idiopathic pulmonary fibrosis presented to the hospital for a consecutive double-lung transplant. On postoperative day 27, the patient became increasingly lethargic and unresponsive. He developed acute respiratory distress, involuntary myoclonic movements, anasarca, marked oliguria, and persistent atrial fibrillation. On postoperative day 28, the laboratory reported mold growing in pleural fluid. Intravenous amphotericin B was started. A magnetic resonance imaging (MRI) study without contrast was performed, which showed numerous supratentorial mass lesions, the largest measuring 2.5 cm in greatest dimension, with minimal surrounding vasogenic edema and mild local...
mass effect. There were scattered areas of susceptibility artifact, which suggested a microhemorrhagic component (Figure 4a, 4b). Cultures from a tracheal aspirate and the surgical incision site grew mold, but blood cultures remained negative.

Five days after the first MRI without contrast, a second was performed, which showed progressive interval growth of the previously identified lesions and the development of additional lesions (Figure 4c, 4d). It was determined that these lesions were most likely opportunistic or fungal in origin. The patient’s family consented to the withdrawal of care, and he died under comfort measures. The mold from pleural, tracheal aspirate, and incision site cultures was identified postmortem as *S. apiospermum*.

Relevant autopsy findings included dull pleural lung surfaces with thick fibrinous exudate that was microscopically found to contain large branching septate hyphae. Fungal abscesses with prominent angioinvasion were seen in the kidneys, outer portion of the aortic wall, thyroid gland (Figure 3b), brain, and heart (Figure 2b). Postmortem lung cultures grew *S. apiospermum* and *Cladosporium* spp.

**DISCUSSION**

These two patients portray the clinical and autopsy manifestations of disseminated *S. apiospermum* infection (Table 1). Both had early signs of rapidly changing mental status with corresponding changes in brain imaging studies. Myocardial abscesses were found at autopsy in both cases, which might have allowed for rapid dissemination to multiple organs. Myocardial wall abscesses by *S. apiospermum* are uncommon, and only a few have been reported (4).

Patients may acquire *S. apiospermum* via inhalation of fungal conidia, traumatic inoculation of the skin, or...
colonization of the upper respiratory tract. It is unclear which of these caused the infection in the patient in Case 1, as both lung and skin lesions were present. The skin lesions provided the opportunity for morphologic characterization in the first patient, and correlation with the blood culture allowed for diagnosis of disseminated, invasive *S. apiospermum* infection. In Case 2, possible sources of infection include inhalation, inoculation of the surgical wound site, or tracheal colonization. Tracheal colonization has been described in patients with cystic fibrosis (3). Colonization is a less likely source, as this patient did not have cystic fibrosis or a history of this infection. In our opinion, inhalation or inoculation of the patient’s surgical wound is the most likely source of infection. Surgical intervention was not performed on either patient.

Prognosis following disseminated infection is dismal. In both of the patients in this series, myocardial wall invasion presumably led to dissemination throughout several organs, including the brain. *S. apiospermum* is known to be relatively neurotropic, usually due to hematogenous spread from a primary focus (2, 5). Due to morphologic and clinical similarity to the widely prevalent *Aspergillus* and frequently negative blood cultures, *S. apiospermum* infections are often identified late in the course of disease.

Infection by *S. apiospermum* is exquisitely difficult to treat. Empiric therapy for a suspected disseminated fungal infection may include an echinocandin, an azole, and/or amphotericin B (6). *S. apiospermum* is innately resistant to amphotericin B, and the current treatment of choice is voriconazole in combination with an echinocandin (7–9). In vitro studies have shown a synergistic effect of these two antifungals (10). When feasible, this treatment should be combined with surgical debridement (11, 12). The use of voriconazole in cases that involve central nervous system (CNS) infection is particularly important, as it has increased CNS penetration compared to amphotericin B, echinocandins, itraconazole, or posaconazole (8). Due to wide variation in antifungal resistance, susceptibility testing can be useful (11). However, this testing is not available in many laboratories, and the rapid disease course makes it unlikely that sent-out laboratory results will be of
value. Moreover, there are no Clinical and Laboratory Science Institute–approved breakpoints for in vitro susceptibility testing for this organism (13).

After the cause of infection was known to be *S. apiospermum*, the first patient was treated with the recommended combination of voriconazole and micafungin, but he did not improve. The lack of response might have been due to the already advanced course at the time of diagnosis. The second patient was treated with amphotericin B monotherapy, as the organism was not identified until after the patient’s death. He was also given inhaled prophylactic amphotericin after his transplant. It has been suggested that antifungal prophylaxis may select for *Scedosporium* spp., as these fungi are generally resistant to the commonly used prophylactic antifungals (1).

**Acknowledgment**

The authors would like to thank Thomas P. Lohmann, MD, for his critical review of this paper.


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**Table 1. Clinical and autopsy manifestations of disseminated *Scedosporium apiospermum* infection in the two patients**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) at death</td>
<td>72</td>
<td>62</td>
</tr>
<tr>
<td>Organ transplanted</td>
<td>Bone marrow</td>
<td>Bilateral lungs</td>
</tr>
<tr>
<td>Underlying disease</td>
<td>Acute myeloid leukemia, cytomegalovirus</td>
<td>Idiopathic pulmonary fibrosis, atrial fibrillation</td>
</tr>
<tr>
<td>Diagnosis of <em>S. apiospermum</em> (days posttransplant)</td>
<td>63</td>
<td>28</td>
</tr>
<tr>
<td>Initially identified source of organism</td>
<td>Skin, blood</td>
<td>Pleural fluid</td>
</tr>
<tr>
<td>Organs involved by <em>S. apiospermum</em></td>
<td>Brain, dermis, heart, lung, liver, blood</td>
<td>Brain, dermis (skin incision), kidneys, thyroid gland, heart, lung</td>
</tr>
<tr>
<td>Interval (days) transplant to death</td>
<td>73</td>
<td>34</td>
</tr>
</tbody>
</table>
Leptospirosis with acute liver injury

John Wysocki, MD, Yong Liu, and Nathan Shores, MD

A 61-year-old man with no significant medical history presented with fever, muscle pain, and weakness. He was found to be in multiorgan failure due to leptospirosis, a condition known as Weil’s disease. A timely workup, combined with early initiation of antibiotics, led to effective treatment for this patient.

Leptospirosis is a worldwide zoonotic infection often resulting from environmental factors such as hurricanes and floods, which are prevalent in the southern USA. The diagnosis is challenging, as the incidence is relatively low in the USA and can often present with highly variable clinical symptoms. The purpose of this report is to remind practitioners of the signs and symptoms of leptospirosis infection so that prompt supportive care and treatment can be started. Mortality from Weil’s disease ranges from 5% to 15%.

CASE REPORT

A 61-year-old man presented with 5 days of fever, pain, and weakness in lower extremities. His vital signs and physical exam were unremarkable. He chronically ingested dietary supplements and Chinese herbal medications. Additionally, he was restoring a house built in southern Louisiana in the late 1800s. His blood work and imaging results from day 1 and day 5 are listed in the Table.

Several infectious diagnoses (bacterial, viral, parasitic) were considered, including leptospirosis. Given the environmental exposures of restoring an old home in the humid climate of New Orleans—which is prone to flooding and infestation with rodents and rodent urine—the patient was at increased risk of transmission. He was started on N-acetylcysteine for his acute liver injury and ceftriaxone for possible zoonotic infections such as leptospirosis. Transjugular liver biopsy revealed increased mitosis and regeneration (Figure 1). Initial results were also suggestive of leptospirosis and were later confirmed by the Centers for Disease Control and Prevention to be Leptospira based upon Warthin-Starry and immunohistochemistry stains (Figure 2). Ten days later, his serum was positive for leptospira antibodies, which normalized with the antibiotics. He recovered fully.

Table 1. Laboratory and imaging results

<table>
<thead>
<tr>
<th>Test</th>
<th>Day 1</th>
<th>Day 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count × 10⁹/μL</td>
<td>5.7</td>
<td>9.3</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>14.4</td>
<td>11.1</td>
</tr>
<tr>
<td>Platelets (cells/mm³)</td>
<td>33,000</td>
<td>31,000</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dL)</td>
<td>54</td>
<td>41*</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>4.9</td>
<td>3.2*</td>
</tr>
<tr>
<td>Creatine kinase (U/L)</td>
<td>8000</td>
<td>4500</td>
</tr>
<tr>
<td>Total bilirubin (mg/dL)</td>
<td>1.1</td>
<td>29</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/L)</td>
<td>77</td>
<td>245</td>
</tr>
<tr>
<td>Aspartate aminotransferase (U/L)</td>
<td>403</td>
<td>453</td>
</tr>
<tr>
<td>Alanine aminotransferase (U/L)</td>
<td>216</td>
<td>355</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>1.2</td>
<td>1.6</td>
</tr>
</tbody>
</table>

Table continued

| Abdominal ultrasound with Doppler | Gallbladder sludge, No gallstones, Normal biliary ducts, Patent vessels, Splenomegaly |

* Required temporary dialysis.

DISCUSSION

Leptospirosis is a worldwide zoonotic infection due to Leptospira spp. Animals, specifically rodents, are the primary vectors of disease. Human infection results from exposure to the urine of infected animals or through contact with contaminated soil or water. Regions prone to hurricanes and floods are at higher risk of exposure (1–3). The diagnosis is challenging for several reasons: 1) its low incidence in the United States, 2) its highly variable clinical symptoms, and 3) its mimicry of common diseases such as viral hepatitis.

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Typically, leptospirosis has a biphasic disease course. The first phase lasts up to 7 days and presents with unspecific symptoms such as fever, headache, and myalgia. The second phase can be categorized into anicteric and icteric forms. Most patients undergo the milder anicteric form. Rarely, leptospirosis presents with a severe icteric form with multiple organ involvement called Weil's disease. Weil's disease can lead to acute kidney failure, acute liver failure, rhabdomyolysis, and thrombocytopenia with possible hemorrhagic diathesis. Its mortality rate ranges from 5% to 15% without treatment. Transaminase levels are moderately elevated in the 100s IU/L, with a mild increase of alkaline phosphatase (1). An aspartate aminotransferase–alanine aminotransferase ratio of >3 may indicate a poorer prognosis (4). Serum bilirubin may rise as high as 30 to 40 mg/dL (1). Jaundice as a result of septic cholestasis typically appears during day 5 to 9 of the disease course. Liver function usually returns to normal without complications, as observed in this patient.

The diagnosis can be confirmed by serological tests detecting leptospiral antibodies or through polymerase chain reaction assay (1). Pathologists may also perform leptospiral immunohistochemistry staining on liver biopsies for diagnosis, but this must be specifically requested (5).

Treatment of leptospirosis with antibiotics remains controversial (6). A Cochrane review of 7 randomized clinical trials was inconclusive on the role of antibiotics (penicillin) in leptospirosis, regardless of severity (7). Nearly 90% of cases are considered mild, and oral doxycycline or amoxicillin may be used. For severe cases, parenteral high-dose penicillin G or ceftriaxone is recommended (8).

Torus palatinus

Muthiah Vaduganathan, MD, MPH, Ariel E. Marciscano, MD, and Kristian R. Olson, MD, MPH

CASE DESCRIPTION

A 78-year-old Asian-American woman was incidentally noted to have this 3 cm mass on the roof of her palate during hospitalization for right lower lobe pneumonia (Figure). The patient reported no symptoms related to this mass, which was present since her teenage years. She stated that her mother and one maternal relative had similar lesions.

DISCUSSION

Tori are benign bony outgrowths from the mandible and hard palate that are relatively common, with a prevalence of roughly 27 of 1000 adults (1, 2). Torus palatinus, or oral exostosis, generally occurs along the midline, while torus mandibularis appears on the lingual surface and is often bilateral. Tori are more common in females and in specific ethnic and racial groups, especially Asians (3). The underlying pathogenesis is thought to be largely genetically driven (4), but local stressors and micro trauma may be contributory (5). Tori have a benign natural history and are slow growing and noninvasive. Removal is required only if they are symptomatically burdensome or interfere with denture placement in edentate individuals. It was determined that her relatively small, broad-based, multilobulated torus did not confer increased risk of aspiration. Surgical correction of the mass was considered but deferred given her age, comorbidities, and lack of evident symptoms.

Baylor Medical Center at Garland celebrates a half-century of service to our community

Baylor Medical Center at Garland recently celebrated the hospital’s 50th anniversary. Named in honor of World War II veterans, the 100-bed Memorial Hospital of Garland opened its doors on March 16, 1964. In January 1991, the hospital joined Baylor Health Care System, becoming Baylor Medical Center at Garland. What began as a humble not-for-profit community hospital has now grown into an expansive medical facility offering a full spectrum of health care services, including extensive heart and vascular services, a breast center, and a newly designed emergency department, to name just a few.

“With each passing decade, we’ve found new ways to improve our hospital and invest in our community by expanding our services and striving to improve patient care,” said Tom Trenary, president of Baylor Garland. “And every step has been guided by the values of Baylor Health Care System—integrity, servant-hood, teamwork, excellence, innovation, and stewardship.”

Baylor expertise at Walgreens in-store clinics

HealthTexas Provider Network recently signed a deal with Walgreens to provide medical oversight of advanced practitioners (e.g., advanced nurse practitioners and physician assistants) at in-store clinic locations. The retail health care concept represents transformative health care changes in North Texas.

“This will provide convenient access for low-level care after hours and on weekends,” explained Gary Brock, president and chief operating officer, Baylor Scott & White Health-North Texas. It’s also a cost-cutting idea, he said. “Having more touch points, in a lower-cost environment than what you would see in our own primary care physician offices and hospitals—that means an improvement in our cost profile.”

The Walgreens clinic facilities are currently being designed and built inside existing stores. The name is simple and direct: Health Care Clinic at Walgreens. The target for opening is August 2014. The clinics will be strategically located throughout the Dallas-Fort Worth market. Thirteen are planned, but it’s possible the number will increase.

BHVH earns prestigious 2014 TAPE Award

The Baylor Jack and Jane Hamilton Heart and Vascular Hospital (BHVH) is a 2014 recipient of the Texas Award for Performance Excellence (TAPE) from the Quality Texas Foundation. The TAPE award is the state’s highest honor for quality and organizational performance. BHVH earned this award by demonstrating exceptional performance in all areas of organizational management.

The TAPE program is run by the Quality Texas Foundation and is modeled after the Malcolm Baldrige National Quality Award, using its criteria and process. BHVH was thoroughly examined, including site surveys and numerous reports on all levels of operations. “The next step on our journey will be the pursuit of the Malcolm Baldrige National Quality Award. I am confident that with this team, we can accomplish anything,” said Nancy Vish, president and CNO of BHVH.

BHVH was previously honored at the achievement level by the Quality Texas Foundation in 2011 and 2012. Past Baylor TAPE award recipients include Baylor Medical Center at Waxahachie, 2012; Baylor Medical Center at Irving, 2011; Baylor Regional Medical Center at Plano, 2010; and Baylor Regional Medical Center at Grapevine, 2009.

Game on: Baylor research study wins first place in national competition

A gaming study from Baylor Scott & White Health won a first-place award at the International Meeting on Simulation in Healthcare. The research, which was sponsored by the Agency for Healthcare Research and Quality, began as a unique collaboration with the University of Texas (UT) Arlington and UT Dallas in 2011. Using interviews conducted with Baylor nurses and physicians, the project team developed a learning curriculum within a video computer game that simulates interactions between physicians and nurses—otherwise known as GLIMPSE (Game to Learn Important Communications Methods for Patient Safety Enhancement). Three years after the start of that collaboration, the project team has tested the completed game at four patient care units at Baylor Irving.

From the onset of this project, the study’s creators had set their sights on one very important goal: to improve the patient experience. “A great deal of health care errors are due to miscommunication between physicians and nurses, which can present patient safety issues,” said Susan Houston, PhD, RN, director of nursing research and collaborator in the GLIMPSE project. “The nurses as well as the physicians at Irving who played the game were extremely supportive,” she said. “Overall, the collegiality and collaboration have been wonderful in an effort to pull off this 3-year project. Ideally, we will see the long-term effects, not only just in the results of this study, but through a marked decrease in health care errors that occur due to miscommunication.”

Three Baylor hospitals on Consumer Reports top 5 safest ratings

Three Baylor Health Care System hospitals are among the top five hospitals in the Dallas–Fort Worth area based on safety scores, according to the Consumer Reports Health Hospital Ratings. Out of the 47 hospitals rated in the area, only Baylor Waxahachie scored above 70 on the 100-point scale. Baylor All Saints Medical Center at Fort Worth earned the number two rating, with an overall score of 61, while Baylor Medical Center at Irving was fifth on the list, with a safety score of 59. The ratings combine five key measures—mortality, readmission, overseer of CT scans, hospital-acquired infections, and communication—into one composite score so consumers can easily compare hospital safety.

“Baylor strongly supports efforts by Consumer Reports to provide information to the public to help them make informed choices about their hospital care,” said Donald Kennerly, MD, associate chief quality officer for Baylor Scott & White Health. “We are proud that three of the top five highest-rated hospitals in the Dallas–Fort Worth area are Baylor hospitals. Baylor has made major investments over many years to improve the quality and safety of care we provide our patients.”

Heart disease secrets may lie beyond the heart

For the first time ever, new research suggests that the most common forms of heart disease may be detected in organs outside the heart. If future studies confirm those findings, cardiologists might someday diagnose a person’s heart disease risk with a heart scan, cholesterol test, and urine sample. The latest study, from Baylor’s metabolic research ranks,
was published in the *Journal of the American Heart Association*.

Led by Raphael Schiffmann, MD, director of Baylor’s Institute for Metabolic Disease, part of Baylor Research Institute, the study found that increased levels of the urinary substance Gb3 could mean a patient is at higher risk for near-term death from heart disease. Originally, the trial was designed as a screening study for Fabry disease, a rare genetic condition that triggers heart problems. Dr. Schiffmann and his team tested the urine of patients to find elevated Gb3 levels, which is common in Fabry disease patients. “To our surprise, we noticed after a few months that some heart disease patients who did not have Fabry disease did have elevated Gb3 in the urine,” Dr. Schiffmann said. “We also found that some of those patients had died in the short interval that had passed since we had last seen them for this screening study.”

Using statistical data, Dr. Schiffmann and his team found that heart disease patients with higher Gb3 levels face a higher risk of death than those with normal amounts of the biomarker. “This was a very surprising, yet encouraging, discovery, given the fact that Gb3 elevation was—until now—thought to be the exclusive hallmark of Fabry disease,” Dr. Schiffmann said. “Remarkably, this biomarker is significantly different from existing ones and could be of great significance for the future study of heart disease.” Continued research is needed to fully explore heart disease biomarkers.

**Baylor awarded patent for major advance in islet cell transplant research**

Baylor Research Institute (BRI) has been awarded a patent from the US Patent Office for a potential strategy to improve the outcomes of islet cell transplantation for patients with type 1 diabetes and chronic pancreatitis. The Baylor research team determined that withaferin A (WA), a plant-derived compound with strong antiinflammatory and antioxidant properties, is a strong inhibitor of the inflammatory response in islets, protecting them against cytokine-induced cell damage while improving the survival of transplanted islets. The results suggest that WA could be incorporated as an adjunctive treatment to current immunosuppressive therapies to improve islet transplant outcome.

“Currently, no antiinflammatory compound with broad benefits such as withaferin A is used in the islet transplant field. The experimental research performed at Baylor on this compound has improved the basic understanding of the molecular mechanism involved in islet damage during the peri-transplant period,” said Bashoo Naziruddin, PhD, director of the Islet Cell Laboratory at Baylor University Medical Center at Dallas.

“Islet cell transplant continues to show promise for treating patients with type 1 diabetes. Auto islet cell transplant already is used successfully to treat patients with chronic pancreatitis,” Dr. Naziruddin said. “We hope the use of WA will strengthen existing immunosuppressive strategies to improve current islet transplant outcomes by preserving the mass and function of engrafted islets.”

**BRI receives $3.3 million grant to continue research in autoimmune diseases**

BRI has received a $3.3 million grant from the National Institute of Arthritis and Musculoskeletal and Skin Diseases to fund its Autoimmunity Center of Excellence. The grant was a renewal awarded to Virginia Pascual, MD, the leader of the Autoimmunity Center of Excellence and a director at Baylor Institute for Immunology Research (BIIR). The BIIR Autoimmunity Center of Excellence is one of only a few such centers in the nation. This designation is given to outstanding research and clinical facilities that are awarded these grants.

“This was an extremely competitive grant, and we are fortunate that our proposal was renewed. The goals of the center include understanding the mechanisms that lead to...
autoimmunity and developing tools to monitor these dysfunctional pathways in patients," Dr. Pascual said.

"BRIR has a very strong autoimmunity program, and the renewal of the Autoimmunity Center of Excellence further demonstrates the quality and success of our program," said Michael Ramsay, MD, president of BRI. "Dr. Pascual’s research focuses on autoimmune diseases such as lupus, dermatomyositis, and juvenile arthritis. Her work on juvenile arthritis led to a successful treatment for children who did not respond to other therapies. Her group identified an immune system protein, interleukin-1, which is overproduced in these children, and found that a drug that was already on the market could block the effects of this protein."
James Walter Fleshman Jr., MD: a conversation with the editor

James W. Fleshman Jr., MD, and William C. Roberts, MD

James Fleshman (Figure 1) came to Baylor University Medical Center at Dallas (BUMC) as chief of surgery and as the Helen Buchanan and Stanley Joseph Seeger Endowed Professor and Chairman in 2012. He was born on August 2, 1954, in New Orleans, Louisiana, and grew up in various southern US cities, in St. Louis, Missouri, and in Northern Ireland, which he loved and allowed him to do a good bit of traveling in continental Europe. He received his bachelor’s degree from Washington University in St. Louis, Missouri, summa cum laude, and received his medical degree 4 years later from Washington University School of Medicine. His training in general surgery was at the Jewish Hospital of St. Louis, a part of Washington University School of Medicine. He did a fellowship in colon and rectal surgery at the University of Toronto in Canada. After returning to St. Louis in 1987 as a member of the Section of Colon and Rectal Surgery of Washington University School of Medicine, he rapidly rose through the ranks to become full professor of surgery in 2000. When he came to BUMC in 2012, he was also made professor of surgery at Texas A&M Health Science Center.

Not only has Dr. Fleshman been a very active and creative surgeon, but his research accomplishments have been many. They have resulted in at least 163 publications in peer-reviewed medical journals, 34 articles in non-peer-reviewed journals, and 53 chapters in various books. He has served on numerous governmental and nongovernmental research committees and has been visiting professor through the years both in the US and in other countries. He has developed an international reputation in the laparoscopic treatment of colorectal cancer, the training of surgeons in the laparoscopic resection of colorectal problems, and the development of randomized controlled trials to evaluate the use of laparoscopic techniques in the treatment of colorectal cancer. He has served as president of the American Board of Colon and Rectal Surgery, president of the Research Foundation of the American Society of Colon and Rectal Surgeons (ASCRS), and president of the ASCRS. He and his lovely wife, Linda, are the proud parents of three offspring, Brett, Cindy, and Angie. James Fleshman is also a good guy and a pleasure to be around.

William C. Roberts, MD (hereafter, Roberts): Dr. Fleshman, I appreciate your willingness to speak to me and therefore to the readers of the BUMC Proceedings. To start, could you talk about your early life, your parents, your siblings, and your schooling?

James Walter Fleshman Jr., MD (hereafter, Fleshman): I was born in New Orleans, Louisiana (Figure 2). My mom and dad were both college educated, the first ones in each of their families, and at the time I was born they were students in the New Orleans Baptist Theological Seminary. We lived in student housing in Gentilly for about 3 years, and then we moved to Luling, Louisiana, a small blue-collar, engineering community where most worked for a subsidiary of Monsanto. My dad, a mechanical engineer, was in the army during the Korean War and was stationed at Fort Dietrich, part of the biological weapons development program. He made the processes that were eventually used to develop biological weapons, something he’s not particularly proud of, and the work probably also affected his late-in-life health because of receiving many vaccines as a guinea pig. We lived in Luling until I was 6 years old. We attended a small church where my parents, who had a partial degree in theology, served as deacon, librarian, and head of the children’s department. I became friends with the pastor’s son. As an only child, I relied heavily on friends as companions. My mom and dad then moved to Shreveport where my dad worked for the American Manufacturing Foundation (AMF), the company that initially made the pin-sporters for bowling. The Shreveport subsidiary, AMF Beard, made liquefied petroleum gas (LPG) tanks for the oil and gas industry. We lived in Shreveport for 7 years.

At the end of my eighth grade year, we moved to a little town called Bangor County Down in Northern Ireland, sister city of Bangor, Maine, and lived there for 5 years. It was a small oceanside community with some vacation homes. I attended Bangor Grammar School, an all-boys college preparatory school, starting in second form (their name for grades), and I went all the way through lower sixth form. All my high school years
were spent there. I learned how to play rugby and cricket, ran track, and excelled in science and math, but not in languages. I loved that school. I finished as the “head boy,” meaning that I was elected by the faculty to lead the prefects and also to be the student representative to the faculty. The “prefect system” goes back to John Brown’s schoolboy days. The boys did the discipline of each other, patrolling the hallways, making sure all students got to class on time and were not misbehaving, and meting out punishments (for example, writing school rules a certain number of times).

We attended an Irish Baptist church, and I became very active in the youth group. During one summer I did a mission trip to Southern France for 8 weeks, selling Billy Graham books and talking to strangers. It was an outstanding experience.

In November 1971, we moved back to the US, to Kirkwood, Missouri. My dad had worked there earlier for 18 months. My parents reacquainted themselves with previous friends. (Kirkwood was the first designed community development in the US and was located 12 miles from downtown St. Louis. In the early 1900s, it was a getaway for people living in St. Louis.) We lived there during the 4 years I attended Washington University. I did a premed biology honors degree and did research with a professor of neuroanatomy, Ted Jones. I was actually part of the original experiment on mapping the cerebral cortex. (I am starting to read about it in my current master’s degree classes in education at Southern Methodist University.) We mapped the cerebral cortex of the Macaque monkey and the domestic cat. My honors thesis for biology was the developmental process of the fetal and neonatal rat cortex using Golgi staining, looking at the progression of axonal migration. We could tell when the midbrain and the hindbrain were communicating with the cerebral cortex and in what timeframe. Dr. Jones was an MD, PhD, from New Zealand. He ended up at the University of California at San Diego as chair and professor of neuroanatomy. He and I got along well because he played rugby in college as did I.

I met my wife, Linda Lewis, at Kirkwood Baptist Church when we were in the choir together. We dated through college off and on. We married in July 1976 after graduating from college.

Roberts: You must have been a fast runner to play rugby? What did you do in track?
Fleshman: I was a long-distance runner.
Roberts: Do you still run?
Fleshman: I quit about 7 years ago when I had my first deep-vein thrombus and pulmonary embolism. My lung capacity isn’t what it used to be. I had pulmonary emboli in multiple segments of both lobes. I got that from too much air travel. I was on a flight to Istanbul, which was diverted to Shannon, Ireland, and ended up being 15 hours long. I am sure that I got the clot while on the plane. When I got to Istanbul, I took a nap, went for a run, and did okay until after returning to New York. I could hardly make it up the escalator in the New York airport. I then went to my physician in St. Louis. He thought maybe I had asthma. No one thought about deep-vein thrombus because my leg didn’t hurt and it wasn’t swollen. I went 3 months before the diagnosis was made with an ultrasound and chest computed tomography. I got on anticoagulants and am still on them.

Roberts: Was that the first time you had any health issues?
Fleshman: Yes.

Roberts: It sounds like your childhood was a pretty happy period. Did you get along well with your mom and dad?
Fleshman: My mom and dad were good strong Christian people. My dad and I got along really well. He was always involved with my projects and I with his projects. He was a minor league baseball player when he was in the army in Frederick, Maryland. I inherited his love of baseball (Figure 3). When I was in junior high I was a catcher, and I played softball until I was almost 50.

Roberts: Could you hit?
Fleshman: My father made me a left-handed hitter even though I’m a right-handed thrower. I couldn’t hit it a long way but I could get on base almost every time. I played outfield in softball because I was a fast runner.

Dr. Jones got me into Washington University Medical School (Figure 4). In my senior year of college he took my resume to Max Cowan, associate dean of admissions at the time, and I was accepted into the 1976 class. I was also accepted into several other medical schools but declined. Medical school was a very interesting time. Linda and I were married and had our first child, Brett, during my neuroscience final (Figure 5).

Roberts: What’s Brett’s full name?
Fleshman: James Brett, born May 3, 1977. He was a hon-
eymoon baby. He and I got along well. He was a great kid. He also graduated from Washington University but with a business degree. He is now director of new business development for a pharmaceutical company in Raleigh, North Carolina. The company sells drugs for patients with chronic obstructive lung disease. His next move will be a vice presidency position. He is 37 this year. He is married to his college sweetheart, Kara, and they have four kids (Figure 6). I have three granddaughters (Maren Emily, 7; Livia Jane, 4; Whitney Susan, 2) and one grandson (James Michael, 6 months). My grandson is fifth-generation James Fleshman. My dad’s uncle was James, I’m a Jr., and Brett is actually James Brett.

Roberts: Back a minute to your early life. It sounds like you enjoyed school. Did studies come easy for you?

Fleshman: I loved them. When I was in first grade I couldn’t read. My mom had to work with me constantly. I was a very slow reader and got words reversed.

Roberts: Would that be dyslexia today?

Fleshman: I don’t know, but the neuroplasticity class I’m taking suggests that I had to rebuild some connections in my brain before I got it. I spent a lot of time reading The Cat in the Hat-type books. I read constantly during the summers. Mom took me to the library religiously.

Roberts: Do you read fast now?

Fleshman: I do okay. I can get through a 250-page book in probably 3 days.

Roberts: In your early schooling, were there any teachers who had a major influence on you?

Fleshman: Yes, my second grade teacher at Arthur Circle Elementary School in Shreveport, Louisiana, Ms. Lynch, one of the sweetest people I have known, and my third grade teacher, Ms. Jeffcoat, gave me the love and support that I needed to get over the reading problem. By the time I was in junior high, I was in an accelerated class. My class took the California Aptitude Tests, the first group to do that in the 1960s. The students were screened based on those tests. I was in the advanced class by the seventh grade. The education system was experimenting, and the advanced class was structured differently, with projects, self-directed instruction, and “modern” math. Students were on their own to learn. I relied on my dad to help me. My mom was not a mathematician. I had to work hard and I wanted to excel.
Roberts: When you brought your report card home, did your parents comment much? Did they congratulate you?

Fleshman: I got in trouble if my grades weren't all As. My mom and I had a lot of disagreements on my performance at school. She is a perfectionist.

Roberts: You felt pressured to excel?

Fleshman: Yes.

Roberts: You mentioned that your father would get you involved in his projects. Did that eventually help you in surgery?

Fleshman: Yes, I think it did. It made me love working with my hands. We built a camping trailer together from scratch. He welded the frame and then he and I built the wooden top to it and put all the segments (taken from a Popular Mechanics design) together. We built that when I was in grade school. He taught me how to hammer, nail, and saw. His dad had been a mechanic and ran a generator restoration shop for car generators and alternators. They would take them out of the car, clean them, rewrap the wires, and put them back in. I worked in his shop several summers as an 8- and 9-year-old. My maternal grandfather owned a construction company before the Depression. When I knew him he was doing handyman jobs. I messed around in his workshop.

Roberts: Did you have other odd jobs?

Fleshman: I mowed yards during high school and college. There weren't many places in Northern Ireland to do odd jobs because of the strong unions. When we returned to the US, I started my own lawn-mowing company. I would mow 30 to 35 yards a week. Basically, I put myself through college. I had a Sears self-propelled, 27” blade push mower and then a Toro, a straight push mower. I got to where I could mow a yard in 30 minutes. I also had a manual push edger. The summer mowing would last through October in St. Louis.

Roberts: In the summers you usually had a job?

Fleshman: Yes. I worked at Baskin Robbins for two summers, making $1.10 an hour, barely enough money to take Linda to the movies with a week's worth of work. I was in college at the time. She was at DePauw University in Greencastle, Indiana. I would work really hard during the week and visit her on weekends, two or three times a semester.

Roberts: How far a drive was that?

Fleshman: It was a 3½-hour drive from St. Louis. We dated for the first 2 years and broke up for about 18 months. Then I realized that that was the stupidest thing I had ever done. It took a lot of groveling on my part to get back into her good graces, but it was worth it. She is the love of my life. During my sophomore through senior years, I worked on my honors project in college in Ted Jones’ lab during holidays and summers.

As an undergraduate at Washington University, I spent 1.5 years working at the Jefferson Barracks Veterans Administration Hospital in St. Louis for an endocrinologist doing thyroid gland research. (They had just discovered how to isolate DNA in 1972.) We would harvest the cerebral cortex of dogs, inject them with radioactive iodine and thyroid hormone into the isolated carotid artery, and then harvest the cerebral cortex and take different parts of the brain and isolate DNA. We'd take the pellet and look into the different components of the cellular pellet versus the cytoplasm to see where it ended up. It wasn't a well-thought-out process, but it did prove to me that thyroid hormone doesn’t do a whole lot up in the brain. The one thing we didn’t know about was the interaction between thyroid-stimulating hormone and intercerebral function. The cerebral cortex doesn’t take up a lot of thyroid hormone.

Roberts: When did you realize that you wanted to be a physician?
Fleshman: On the trip to Northern Ireland I read a book by William Nolen entitled *The Making of a Surgeon* about his time at Bellevue Hospital as a resident. I realized I wanted to be a doctor after reading it. The concept was fixed in my mind during an incident in high school. I had just finished rugby practice. I was 16 and had just completed my Boy Scout Life Saving Training (a first aid course). While lining up to get on the bus, a 12-year-old was pushed into the wheel well at the front of the bus. The wheel turned and caught his leg in the wheel well, slicing open the inside of his thigh. We got the bus driver to turn the wheel so we could get him out and laid him on the ground. He was losing a lot of blood. I remembered the femoral artery pressure points. I held it for about 30 minutes until the ambulance arrived. Every time I would release the pressure to allow blood back into his leg he would scream because of the pain. I couldn’t put a tourniquet on him because the tear was too high up on his groin. I just held my thumb over the artery. They were able to save his leg. I remember thinking that it was pretty cool and I could do that. That sort of solidified my wish to be a physician. I spent my senior year in high school doing physics, chemistry, and biology.

Roberts: *It sounds like your spending part of your teenage years in another country proved most exciting.*

Fleshman: Those years were formative. I love Northern Ireland. I made many friends and traveled to continental Europe multiple times. I spent a summer in Switzerland at a Ranger camp. We hiked or skied on Lake Geneva. I spent a summer in France when I was 14 and also visited Belgium and Holland. I had orthodontic work during this time and had to go to London every 3 months to have adjustments made. I spent the weekends with a friend of my dad’s family, and we would tour London. It was terrific. At the time we were studying Lord Nelson and the Battle of Trafalgar, we visited Trafalgar Square and the museums. When I was 15, with the same family, we made a biking tour through Normandy on the 25th anniversary of World War II. (Their son is Sam Haynes, now a history professor at the University of Texas at Arlington.) We rode down the beach road where there were still bunkers and burned-out equipment, and we walked out on the beach where there were iron crosses. Mrs. Haynes made us watch *The Longest Day* with John Wayne and Robert Mitchum. I remember the story of that so well because we went to Pointe de Haute, where they scaled the wall at night. We were on Omaha and Juno Beaches. We spent time on Mont Saint-Michel, which is an island that sticks out into the Atlantic and is not accessible at high tide. It has circular streets that climb to the top of the mountain, where a classic medieval castle sits.

Roberts: *When were home with your parents, did you have dinner together?*

Fleshman: We tried. Usually my dad would get off at 5:00 PM. My mom would be upset if he was late.

Roberts: *What were your dinner conversations like?*

Fleshman: We discussed politics, school, church, my behavior. We had a border collie named Twinkle Toes.

Roberts: *What did your father do after dinner at night?*

Fleshman: For several years he worked on a master’s degree in cryogenics. Because he worked with LPG tanks, he learned how natural gas was transformed into liquid. He had to know what cold did to structure. He utilized what he learned in seeking that degree in his work. In Ireland he was in charge of the tank building section for AMF Beard. They were getting prepared to receive oil and gas from the North Sea in 1967. The European governments had divided up the North Sea into a grid. England and Holland got the Western side, and Sweden, Norway, and Russia, the Eastern side. The Eastern side struck natural gas and the Western side didn’t. We came back to the US in 1972 because there was no petroleum industry to support.

Also, at that time the Irish conflict was at its worst. They were exploding bombs in Belfast. Several checkpoints by the British Army and the Ulster Defense Force were set up. In the fall of 1971, they blew up a car on the main street of Bangor, our little resort town. It blew out all the windows in the entire street. Because Bangor had a mixed religious population—Catholics, Protestants, Jews, and Hindus—we just got along. But it started becoming more intense, including fights on the school grounds. As a prefect, I was responsible for breaking up those fights. It helped to be 6 feet tall when I was 15. No one would mess with me. The Northern Irish in Ulster had money, and their economy was strong. Catholic Southern Ireland was so poor that they had no positive outlook whatsoever. This brought out the class conflict. At the same time, in the US, we were going through the civil rights movement. We left the US in the fall of 1967, the same year that my school was integrated.

Now the people of Southern Ireland are happy as a result of the European Union’s investing a ton of money into their infrastructure. They don’t care what religion you are. They get along with everyone. Now, they have the most educated workforce in the world. That’s why technology companies have moved over there and why so much computer programming is based there.

Roberts: *Why did their banks go broke over there in the last 5 years?*

Fleshman: They overspent. They subsidized loans thinking the good times would not end. People extended themselves beyond what they could afford. There were a lot of foreclosures in Europe, same as in the US, but they were hit harder and faster. Now, they are bouncing back faster than in the US.

Roberts: *What was your home like? Were there a lot of books around your house?*

Fleshman: Yes. My parents now live in Martinsburg, West Virginia, and there are no open surfaces without books on them. My mother is a librarian, so she loves books. My wife doesn’t like us to have a lot of clutter, so I read a book and put it back on the shelf. When we moved I must have donated 6 bags of books that were on my shelves that I knew I would never read again. Half were paperbacks. I love books and know the ones that I would go back to or refer to. They become friends.

Roberts: *What is your mother’s name?*

Fleshman: Dorothy Naquin, born in 1929. She’s Cajun and grew up in Lafayette, Louisiana. My dad’s name is James Walter, born 1928.
Roberts: Why did they move to West Virginia?

Fleshman: We moved back to St. Louis from Northern Ireland in 1972. My dad started working for American Car Foundry, a major railroad car manufacturing company in St. Charles. The company made center flow cars and liquid hazardous material cars. My dad was an expert in cryogenics and flow. In 1975, Carl Icahn bought ACF. He then sold all the cars currently produced, shut down all research and development and all the manufacturing, and took the money and bought Trans World Airlines. He then proceeded to do the same thing to TWA, eventually selling it to American Airlines. As a consequence, my dad lost his job. He went from there to Houston to National Lead in 1975. President Jimmy Carter then stopped all drilling and pumping of oil and gas on the North American continent to preserve our natural reserves. So National Lead, which was a company that made drill bits for mines and wells, shut down.

My dad bought a barrel-washing company in downtown St. Louis before moving to Houston, and that lasted for about 9 months. My parents lost a lot of money on that venture. It didn't work out. He and my mom had a lot of fights over that one. It was awful. I saw my dad trying to do something he wanted to do and my mom had already lived through her dad's going bankrupt and didn't want to see my dad go bankrupt. It became a self-fulfilling prophecy because she harassed him so much that he couldn't do the job that he needed to do. She didn't want him working all the time and he couldn't spend the time needed at work. While in Houston, after losing his job at National Lead, he ran a nonprofit foundation for head injuries when a family friend's daughter had a head injury. After 2 years they shut the foundation down and my dad got a job working for the American Association of Railroads (AAR) as the safety director for moving hazardous materials across the country. Any time radioactive material was moved from Three Mile Island (New York) to wherever they were dumping it in Wyoming or Idaho, he would have to map out the route and do a safety check on everything. He retired at age 72. AAR was in downtown Washington, DC, in the Senate Building next to the Sam Rayburn building. It was so expensive to live in Washington that they lived out at the end of the commuter rail, which is where Martinsburg, West Virginia, is located.

Roberts: Back to your college days. You went to a great school. Did you live at home while in college?

Fleshman: The first year I lived at home. Tuition back then was $1200 a semester, so I could make that much mowing yards, but I couldn't afford to live on campus.

Roberts: What years did you go to college?


Roberts: How was it? How did college hit you?

Fleshman: I never finished high school. Coming from Northern Ireland, I didn't have a high school diploma. I didn't go back to high school after returning to the US. I went straight to community college for a semester in 1972. I took 6-month courses in precalculus, algebra, English, chemistry, and biology at Kirkwood Community College. I got straight As and then started Washington University. It cost more to go to community college than to Washington University. I made $2500 a summer mowing yards. The second year I moved into the Sigma Alpha Epsilon fraternity house, and I got my room and board paid for by being a house manager doing all the maintenance. In 1975, my parents moved to Houston, so I couldn't have lived at home anyway. Room and board was $700 a semester. Washington University tuition rose to $3500 the next year, to $5000 the next year, and to $7500 my last year. I was able to pay the cost during college. My first year of medical school was $7500 a year, and I worked in the labs. On school breaks, I worked for my father-in-law, who was a construction developer. I got married in 1976 and my wife worked at Monsanto as an accountant and also for her dad as the treasurer. I ended up with only a $15,000 loan at the end of medical school.

Roberts: You paid your way through college and medical school. Were there any teachers in college who had a particular influence on you?

Fleshman: Ted Jones definitely did. Richard Bischoff, my neurobiology teacher, and Evelyn Kirkowski, embryology professor, were influential. We also had courses by Rita Levi-Montalcini, the Nobel Prize laureate for DNA. She worked with Sam Wells to describe multiple endocrine neoplasia 1 and 2. She discovered the retinoblastoma gene.

Roberts: How many students were at the time were at Washington University?

Fleshman: About 1200 a class, roughly 5000 total undergraduates.

Roberts: Do you have any idea where you ranked in your class at graduation?

Fleshman: I graduated summa cum laude. I was in the top half.

Roberts: How did you decide to go to Washington University Medical School?

Fleshman: I wanted to stay in St. Louis, and my fiancé had a job working at her father's company.

Roberts: How did medical school hit you? Were there any surprises when you first started?

Fleshman: The biggest thing about medical school is learning a new 3500-word vocabulary in the first year. I spent hours trying to remember what a word meant. By doing that I learned what I was supposed to learn. I loved anatomy. I spent hours studying anatomy because I felt that was the basis of everything I was going to be doing. Because I loved it so much I became a surgeon. At one point I thought I was going to be a cardiologist, a neurosurgeon, or an endocrinologist.

Roberts: Does that mean that you enjoyed most of the clinical rotations?

Fleshman: I had a good time on just about everything I did. I loved neuroanatomy because I had spent so much time with it doing my honors thesis in college.

Roberts: You had sort of made up your mind that you wanted to be a surgeon when you started medical school?

Fleshman: Yes, probably so. I didn't know if I could lead the rigorous life of a surgeon. My goal was to be the best that
I could be at whatever I did. If surgery was so demanding that I couldn’t do it, I was going to look for something else. Having married as a freshman in medical school, my wife and I had a lot of talks about what I should end up doing. To her credit, she said I had to do what made me happy, since I would be spending my life doing it. If it’s surgery, she would deal with it. And she did. She raised our three kids without me. I worked 120 hours a week as a resident. When I got a job, I was gone on weekends, taking call and operating into the night. I missed half my kids’ sporting events, recitals, etc. They have been very gracious to allow me to stay in my family. Now, we are empty nesters and I really grudgingly give up the time that I can spend with her because we never really had the time together. She was busy with the kids and I was busy at work. Fortunately, we loved each other very much. She is a great support for me.

Roberts: In medical school, did any of the professors have a particular influence on you?

Fleshman: Yes, Roy Peterson, the head of anatomy. During my senior year in medical school, I asked Dr. Peterson if I could do a dissection on a cadaver. A friend, who was going into orthopedics, wanted to do all the joints and I wanted to do the torso. He said yes and we dissected the entire body. We took Zollinger’s Atlas of Surgical Operations and did every operation in the book. I helped him dissect all the joints and ligaments. We had a great time and this cinched my love for surgery. Dr. Peterson had been my clinical anatomy professor from day 1, and he was unbelievable. He wrote the books on comparison of computed tomographic images with cross-sections of the cadaver. He spent his last 20 years doing the comparative slicing.

When I was in clinical rotations my third and fourth years of medical school, I was also greatly influenced by Ira Kodner. He was a surgeon at the Jewish Hospital, and I rotated on his service. He knew how to be a mentor. I was his medical student and later became his boss! And he tells it that way by saying, “Be kind to your medical students because you never know when they might become your boss!”

Roberts: What kind of surgeon were you planning to be by the end of medical school?

Fleshman: I thought I was going to be a general surgeon in a small community. I’m the only physician in my family. Even though I had been in research labs throughout my career, I didn’t think I would ever be in an academic position. I knew that I would never become a professor of anything anywhere. I really believe that God led me through my career because I had no idea and things just sort of happened.

I got a residency in surgery at Washington University at Jewish Hospital. They had two chief residents at Jewish Hospital and four chiefs at Barnes Hospital. The program at Barnes was a pyramid and the program at Jewish was a parallel program, meaning if one started in the program one finished in the program. I took the parallel route, which had the same high standards as the pyramid route. A lot of the surgeons at Barnes and Jewish were in private practice, but each had a full-time faculty appointment. I felt like my education at Jewish was wonderful. The surgeons were highly specialized and the busiest and most respected in town. The surgeons at Barnes were also well respected and did a lot of research. There was a core group at Jewish who also did research, and my chairman, Gordon Philpott, had a lab that did immunology research. He put me into the lab between my third and fourth years, and I stayed for 18 months. (Jewish didn’t have a required research rotation.) I stayed in his lab looking at monoclonal antibodies for colorectal cancer and in the process got some publications that influenced my future career. When he retired, he gave me his lab and his RO-1 grant.

During the residency, Dr. Kodner asked me if I wanted to go into colorectal. I said sure. I learned as a fourth-year resident how to do the ileal pouch-anal anastomosis with Drs. Kodner and Fry at Toronto (Figure 8). Because they convinced me to go into colorectal surgery, I did a 1-year fellowship at the Toronto General Hospital under Zane Cohen, Robin McCloud, Earl Meyers, and Hartley Stern. I came back with a broad-based knowledge on treating inflammatory bowel disease (ulcerative colitis, Crohn’s, familial polyposis). Zane was one of the leading individuals in managing hereditary colorectal cancer.

When returning to St. Louis, I joined the full-time faculty at Jewish, something I never thought I would do. I became an assistant professor of surgery at Washington University. I taught residents, had a fellowship program, and I grew. I ran Dr. Philpott’s lab for 10 years, using it to define some things with...
cancer, and developed new technologies: laparoscopy, adhesion barrier for intraabdominal cancer (carcinomatosis). I served as program director for the fellowship in colorectal surgery, which grew from one to three fellows. I became the chief of colorectal surgery in 1998 and remained in that position until 2012. I transitioned from the downtown Barnes Hospital to Barnes West County and started a program there for general surgery residents and our fellows. We had a cancer center satellite—Siteman Cancer Center, a National Cancer Institute–designated comprehensive cancer center. We built a program for Washington University and became one of the top producing areas of the hospital because it was in an area with well-insured patients and also patients who were willing to come to our facility versus going downtown. We left two fellows at Barnes and put a third at Barnes West and used a rotating system, which eventually became two at Barnes West and one downtown. We were that busy! We ended up with seven surgeons in the colorectal section. We collaborated with Dr. Nick Davidson, a gastroenterologist who had a lab that studied the liver fatty acid–binding protein (LFABP) as a modulator of polyp formation in hereditary cancer. If the LFABP is blocked, the cells cannot absorb fat and then polyps do not form.

Roberts: What is your favorite operation?

Fleshman: It would have to be a laparoscopic total proctocolectomy ileal-pouch anal anastomosis.

Roberts: Would it be appropriate to say that you really brought laparoscopic methods into colorectal operations?

Fleshman: I participated in it. I can't claim it solely. There are a lot of surgeons out there working really hard at it.

Roberts: You've talked about improving surgical quality at BUMC. What do you mean by that? And how are you going to do that?

Fleshman: We now have the National Surgical Quality Improvement Program. Dr. Ron Jones started it, and it has been sputtering along. Ernest Franklin, who was a resident of mine back at Barnes, and I have been working on this. We are hiring extra staff, and we’ve negotiated with the information technology group and they are starting to give us the data that we need. We are going to be able to show surgeons what they are doing. Right now, it will be on an institutional level, and as we build the needed amount of data we will start going to the division level (colorectal, minimally invasive, general surgery) and then eventually to the individual surgeons. This will cause all surgeons to think about how they are doing things. It is not to punish them but to teach them how to improve their methods. Most surgeons are well motivated to fix things and will look to improve their processes. Otherwise, they go around on a daily basis thinking everything is fine.

We’ve also started a Surgical Safety and Outcomes Group that should deal with the daily processes in the operating rooms and on the floors postoperatively. We deal with the issue of data collection: Is it as accurate as we think it is? Is all of the data being captured on every patient? Are the history and physicals covering all necessary information? Are the nursing notes capturing everything? Are the anesthesiologists’ notes and preoperative orders making it to the holding area? Are medication orders going with the patient through the system (presurgery, operating room, postanesthesia care unit, and then floor)? Are we missing any? And we are. The electronic health record was supposed to eliminate a lot of these errors but it has not. That’s what the Surgical Safety and Outcomes Group is looking at. We’ve also looked at the way medical staff (residents, fellows, and attending physicians) write notes.

Roberts: Have you been pleased with the quality of the surgical residency program at BUMC?

Fleshman: The residents here are great. We are making some changes. Our residents do over 1200 cases on average in their 5-year residency. Are they doing the right cases for their training? We also found since we brought Texas A&M into the mix that our residents haven’t really been taught how to teach. Even though they were all medical students once themselves, they’ve had no instruction on how to deal with students. We are working to build a culture or environment where the residents understand they are actually teachers as opposed to students.

Roberts: How many interns do you have now?

Fleshman: Nine a year. That’s categorical. We also take two oral maxillofacial a year and one preliminary. We have 45 categorical residents and 3 preliminary.

Roberts: “Categorical” means what?

Fleshman: It means that they are committed to staying 5 years in surgery. A preliminary resident is only here for 1 year. Oral maxillofacial only do 1 year of general surgery internship, and the preliminary may be from radiology or may be a person who missed matching in the general surgery matches.

Roberts: You are pleased with the quality of the residents?

Fleshman: Yes. The one thing they have not had any expectations on is research. Now all the interns that started the program in July 2013 have a requirement to write and publish a paper by the time they finish their fifth year. We have established a research education program. We are teaching them how to think of doing clinical research, including elements of hypothesis development, control group selection, power calculation, sample size calculation, statistical comparison, and literature search.

Roberts: When you were in St. Louis and had a huge clinical practice, along with teaching and running a lab, what was your daily life like? For example, what time did you wake up in the morning?

Fleshman: I’d say 5:30 AM.

Roberts: What time did you get to the hospital?

Fleshman: By 7:00 AM.

Roberts: What time did you leave the hospital as a rule?

Fleshman: Usually by 7:00 PM.

Roberts: Did you get calls at night?

Fleshman: Rarely. Usually colorectal emergencies or problems require a certain amount of time to manifest themselves. It’s pretty rare to have to go in and operate. That’s usually reserved for people who are bleeding or have bowel ischemia or perforations with stool in the abdomen. Diverticulitis patients are put on antibiotics and then they become an elective-type surgical case. Most problems can usually be managed nonoperatively now at first. The specialty is almost all elective, which is what surgical oncology is. There are few emergencies.
Roberts: What about weekends?
Fleshman: I work every day. My wife accuses me of working 7 days a week. I go in on Saturdays just to make rounds. I’m also the associate editor of Annals of Surgery (for colorectal), so every Sunday I spend a few hours doing new review assignments and looking at reviews that are completed.

Roberts: Who is the editor now?
Fleshman: Keith Lillemoe took over from Bing Rikkers. Bing was the chairman at the Department of Surgery at Wisconsin (Madison).

Roberts: Is David Sabiston still alive?
Fleshman: No, he isn’t. He had a stroke several years ago. Did you know him well?

Roberts: I knew him pretty well. I interviewed him for The American Journal of Cardiology.

Fleshman: His philosophy of training residents permeated residency programs for 20 years. He was at his prime at Duke when I was applying for residency. Sam Wells was his protégé.

Roberts: Sam and I were friends at the National Institutes of Health (NIH). We used to play basketball together late Saturday afternoons after spending most of the day at NIH.

Fleshman: That’s where the pyramid program came from and the idea that the chairman would control your life. The chairman would decide where you would go and decide your career based on who they knew who needed somebody.

Roberts: You can’t get away with being that type of chairman anymore.

Fleshman: No, you can’t. My definition of my job is that I am here to make everyone who works with me successful. That’s the bottom line. It used to be your job to fill chair jobs all across the country. I don’t think the generation that is coming through now looks at surgery training like that at all.

Roberts: Do you have hobbies outside of medicine?
Fleshman: I read a lot. My pleasure reading is history. I’ve read a lot about the Civil War era, the West, medieval times. I follow several authors: Stephen Ambrose (Lewis & Clark expeditions and World War II); Mike and Jeff Shaara (father and son authors who write historical novels), Bernard Cornwell (medieval books and a series on Sharpe Brigade about the England-European war and about King Alfred, the English dynasty).

Roberts: What other hobbies do you have?
Fleshman: Golf (Figure 9).

Roberts: What’s your handicap?
Fleshman: My clubs.

Roberts: Do you play much?
Fleshman: I thought I was going to play every weekend when I got here, but it’s too darn cold or too darn hot. I haven’t gotten to play much, but I used to play one or two times on weekends in St. Louis. I am open to any and all suggestions, invitations, etc.

Roberts: Are you left-handed since you swing a bat left-handed?
Fleshman: I play right-handed. My score is routinely 90. If I play at a Tournament Players Club, I shoot about 110.

Figure 9. Jim golfing.

Roberts: Does your wife play golf?
Fleshman: No. She tried but she isn’t patient enough. I scuba dived for 10 years but had to quit when I got the pulmonary emboli. I snow ski. (Kevin Wheelan taught me how to ski.) I skied from 1976 to 2000 (Figure 10).

Roberts: What do you do now to stay in shape?
Fleshman: I used to jog 6 miles three times a week. Since I quit running I walk. I try to go to the gym once a week and work on core muscles. Since I’ve been here I haven’t done much of anything. It is a work in progress or I see a new wardrobe in my future!

Roberts: Where do you live here?
Fleshman: The Preston Hollow area.

Roberts: Are you happy here? Did you make the right move?
Fleshman: Yes.

Roberts: How much sleep do you need at night to feel good the next day?
Fleshman: Six hours. I’m usually in bed by 10:30.

Roberts: Do you do much medical stuff at night?
Fleshman: I bring home a briefcase every night.

Roberts: Back to the residents. Since they are limited in the number of hours they can work per week now, has that bit into their surgical adequacy when they finish their 5 years?

Fleshman: I don’t think it has. We’ve compensated a lot at the hospital level and at the educator level. At the hospital level, the residents don’t have to start intravenous solutions, draw blood, chase down radiographs, transport patients, or do histories and physicals. In my office, the residents take my...
histories and physicals, scan them into the computer system, and do updates. They don’t know the patient when they come to the operating room most of the time. They know why the patient is there but haven’t spent any time with them. I’d say by eliminating all the scut work, we are probably still getting the same amount of education in the operating room and didactic teaching. The real problem is that some of the judgment issues that you used to get, such as staying with patients when they have a complication and following through the complication, are missing because certain trainees, at least interns, can’t work more than 16 hours in a row. If a patient deteriorates during the day and the residents stayed with them overnight, then they have to go home the next day because they’ve been up for 36 hours. They miss what happens during the day with that patient. The follow-through and the ability to stay and make a 36 hours. They miss what happens during the day with that patient. The follow-through and the ability to stay and make sure a problem is managed are missing.

Fleshman: If we are in San Francisco for a meeting which runs from Sunday through Thursday, I might take Friday and go to Napa. We stayed an extra day in Washington, DC, so we could visit my parents. I haven’t done much international travel since my blood clots. I’ve tried to limit flights that are longer than 7 hours. I’ve accepted a few trips this year. My younger daughter turns 30 this year, and we are thinking about a European trip to celebrate that occasion. We took a trip to Italy with my older daughter when she turned 30.

Roberts: You and your family are quite religious? Do you go to church every Sunday?

Fleshman: We joined Park Cities Baptist when we got here. We try to go every Sunday. I find that it is the key to my mental well-being. I have to remind myself that I am not in this alone. I have to make sure that the Holy Spirit is guiding me in what I do, because if I try to do this by myself I’ll fail. I think the only reason I’m here is because of what God has done in my life. I can’t deny that and can’t let that go.

Roberts: Do you drink alcohol?

Fleshman: I’ll have a glass of wine with dinner if we go out to a restaurant. There was a point in my life where the fun part of going to meetings was to sit in a bar after the meeting was over with my friends drinking a glass of port and smoking a cigar. Now, none of us feel like we can smoke the cigars, and we are too tired to drink the port.

Roberts: Is there anything that you would like to talk about that we haven’t touched on?

Fleshman: Yes. My job as chief of surgery is to help make people around me successful. The thing I am most proud of are the people I have trained and worked with and mentored through my career. I’ve trained over 50 colorectal fellows and have lost count of the residents. Those are the ones that I look forward to hearing from and helping in the future. Several of my former fellows and residents are in Dallas: Ernest Franklin, Toby Dunn, Jennifer Lowney, Clifford Simmang, Lorrie Gordon, and Li Ern Chen. Four others at Children’s Hospital trained or worked at Washington University (Drs. Skinner, Foglia, Menkes, and Bliss). I worked with all of them. I particularly enjoy seeing my junior partners excel in their careers. I learned that from Ira Kodner, who was my mentor and took pride in me. I value those relationships. I also value the national-level friendships that I’ve made—Bruce Wolff (Mayo Clinic), Terry Hicks (president-elect, ASCRS), Mike Stamos (president, ASCRS). Those friendships among surgeons in leadership positions around the country are invaluable. I enjoy going to meetings of the American Board of Surgery, the ASCRS (Figure 11), and the American Board of Colorectal Surgery because I get to see all my old friends.
Roberts: Linda plays a good role in developing these friendships also?

Fleshman: She is an integral part. She didn’t travel as much when our kids were at home, but now she goes with me (Figure 12). As a matter of fact, I kept asking her when she was going to go with me on a trip. Her answer would be to wait until the kids were gone. Somebody has to be home to take care of them. I’m proud of her for sticking with it.

Roberts: It sounds like your kids have all turned out well.

Fleshman: They have. I’m very proud of them. Brett has done well establishing his family and my two daughters at establishing their careers. The youngest (Angie) at 29 went back to school at University of North Texas to get her interior design degree, and Cindy works here in town as product manager for an orthopedic instrumentation company (Figure 13). All have college degrees and are focused on being successful.

Roberts: Can’t beat that. James, thank you. I’m glad you are here at Baylor Dallas.

BEST PUBLICATIONS OF JAMES WALTER FLESHMAN (AS SELECTED BY HIM)


Figure 11. American Society of Colon and Rectal Surgeons presidency, 2010.

Figure 12. Jim and Linda, 2013.

Figure 13. Cindy, Jim, Linda, and Angie.


Gluten free-dom: my journey to becoming an unintentional expert

Anne M. Hoyt, BBA

Gluten: What is it? What does it mean to avoid it? How does it inevitably change one’s life? My daughters and I stopped eating gluten. We took our experiences and morphed them into an entirely new life. One daughter, Taylor Nicholson, and I opened a gluten-free bakery called Unrefined Bakery, and the other daughter, Erin, has become a family physician, with an emphasis on wellness and treating the body as a whole. Unrefined Bakery is an organic, non-GMO allergen-free bakery (gluten-free [100%], soy-free [100%], dairy- and corn-free [99%], egg-free [80%], grain-free, sugar-free, yeast-free, nut-free, etc.). At the bakery, we have the unique experience of learning about gluten from the stories of the people we come in contact with daily. We see the frightened look in their eyes when they enter and their joy as foods are brought back into their lives. This is such a current topic and our approach to food is so unique that we have been blessed with numerous articles being written about us in the Dallas Morning News, New York Times, Living Without, Prevention Magazine, and D Magazine, as well as numerous local print and online publications. This is how I became an unintentional expert on being gluten-free. This story has some basic facts regarding the what, why, and how of gluten and celiac disease, as well as about testing and treatment. But mainly this story is about the heart and soul of going gluten-free.

THE BEGINNING OF OUR JOURNEY: DIAGNOSIS AND SYMPTOMS

When our experience with celiac disease started is a tricky question, because symptoms were there long before we heard the word gluten or knew of celiac disease. A key event, though, was when my youngest daughter, Erin, fell in college and suffered a compound fracture in her ankle. The surgery to treat the fracture led to methicillin-resistant Staphylococcus aureus (MRSA), which settled in the bone marrow of her ankle. This led to harsh drugs and a severely weakened immune system. Even as she conquered MRSA, Erin became sicker and sicker. In essence, she failed to thrive, with multiple infections in the year following her MRSA treatment. As always, her stomach hurt, only worse. She did the best she could with a bland diet of soda crackers, bread, and yogurt, which made her even sicker. Then she began bleeding internally, so to another doctor we went. Since we now know from our customers that they go to doctor after doctor, often never receiving a diagnosis, we were fortunate to receive a quick diagnosis by a relatively young gastroenterologist who asked her about her heritage. Hearing that she was a quarter Swedish, the first and only test he did for her was a biopsy of her small intestine, which found “smushed” villi—the hallmark sign for a diagnosis of celiac disease. Of course, we had been concerned that she had something much worse, so we were thrilled to find that all we had to do was stop eating gluten!

We are a family of nerds, so we researched what this gluten-free thing was all about. As I read Living Gluten-Free for Dummies, I was fascinated to learn that many symptoms I considered to be a natural part of aging fell into the category considered to be nongastrointestinal symptoms. I also discovered that my oldest daughter, Taylor, more than likely had celiac disease as well. As I read through the book, I saw my entire family in the pages. My daughters were seemingly symptomatic from birth. Between the three of us, we experienced many random and differing symptoms.

As early as I can remember, Erin had eczema, dry skin, rough elbows, horrific circles under her eyes, hair and nails that didn’t grow, and constant stomachaches. From the moment she could talk, she talked of her stomach. It always hurt. She often threw up. It appeared to be her symptom. But she always grew, so the doctors weren’t overly concerned. They chalked it up to stress since even at that young age she was already a perfectionist. In 1992, when Erin was 7, we took her to the Mayo Clinic due to her stomach. They only tested for and found an increased liver enzyme, which they deduced must have been an anomaly, but we know now is a symptom of celiac disease.

Taylor had been dairy-free since the age of 18 months due to chronic diarrhea. She had terrible colic until she was 6 months, when I finally introduced food. Based on a doctor’s suggestion, I took dairy out of her diet and found an improvement. Today a doctor would most likely eliminate both dairy and gluten to

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determine the true nature of the diarrhea. We know now that
gluten and dairy intolerances are often found together. Taylor
also continued to have unexplained skin rashes and eczema and
headaches. In later years, she described constipation followed by
explosive diarrhea—irritable bowel syndrome (IBS)—and
always feeling bloated and full, yet hungry.

As for me, I had developed IBS and anemia after my first
pregnancy in 1982 and in my late 20s was diagnosed with
fibromyalgia. I had significant joint pain that moved from area
to area, seemingly without rhyme or reason. I was a migraine
sufferer. By my mid 40s, I began having “foggy brain,” moments
when I simply could not think. There were days at work, as
I was pouring through numbers or intricate thoughts, that I
would simply put the paperwork aside and go on to a differ-
ent task. At times, I even turned the keys to the car over to my
children because I couldn’t assimilate the fast-paced action
of cars merging on interstates and changing lanes. I also had five
miscarriages, two before and three after the births of my three
children. I had attributed all of these failing processes to the
simple fact of aging. I would never have gone to a doctor.

My son believes he has a gluten intolerance somewhere on
the spectrum, but at this point he chooses to ignore it as he
travels the world after being in the military. Many people find
that as long as they keep eating gluten, they can continue eating
it, even as it is likely causing silent but serious health issues that
will raise their ugly heads later in life.

As we learned about gluten and its random and pervasive
impact on the body, it seemed likely that all three of us had
celiac disease. To be quite honest, at the time I didn’t care if I
were celiac or somewhere on the gluten-intolerance spectrum,
since the treatment is the same. Had I known my future, that
I would become somewhat of an “unintended expert,” where I
would tell my story over and over again, and that people would
ask me to write my story, I most likely would have gotten tested.
But, I believed I had an issue. I stopped eating gluten. Like
many of our customers, Taylor and I were self-diagnosed and
then we all became self-taught.

RECTIONS

Rather than feeling sorry for Erin or for each other, we felt
an amazing sense of relief that Erin did not have Crohn’s disease,
or colon cancer, or any of the other scary, life-altering diseases
that had run through our minds. What she had was a disease
that could be cured, or at least strongly improved by simply
changing her diet. What an amazing outcome for a woman
who had grown to be so very sick!

These are Erin’s words when I asked her to tell her tale:

I cannot explain the immense amount of relief I felt on my way
home from that appointment [with the gastroenterologist who
made the diagnosis]. A diet change? How easy is that! No matter
how difficult this change would be, this was the best news I had
heard in a long time. I was going to feel better. Until someone
has felt what it means to be out of control of their day-to-day
health, one cannot comprehend what it means to have some of
that control given back, to be the one in charge of changing the
way you feel, for the better. The diet change was a little daunting
at first (there were not many options in stores or restaurants in
2007), but within a couple of weeks, I was feeling much better.
My energy improved, my weight went back to normal, and my
hair stopped falling out. I felt better than I had in months. And
nothing tastes as good as feeling healthy!

Taylor was thrilled that perhaps she too had found a way to
change her health for the better. Due to an awareness of cause
and reaction, Taylor had already self-selected her own diet by
eliminating nearly 100% of bread and pasta. Taylor said,

With no formal knowledge of a gluten-free lifestyle, my body
knew before my mind what was best for me and my overall
health. I didn’t have the emotional transition that many ex-
perience, because for me, I felt so much better than I had my
entire life, and nothing could make gluten worth it again. My
practical approach was just that. Gluten made me feel badly;
therefore I would no longer eat gluten.

I probably had the most difficult transition of the three of
us. Not only did I love to eat baked food, I loved baking! I was
thrilled to find such an easy solution to Erin’s failing health, and I
jumped on board wholeheartedly. But I was sad. I was that person
who got up on Thanksgiving morning and baked six pies just
so they would be at their very best. I baked as an act of love. I
truly grieved, not for the loss of the food as much as for the loss
of baking. Nor was it easy to watch eating become a process. It
became more like math—did I get enough nutrition through the
proteins, fats, fiber, and carbs? It became a function of eating to
live, eating for proper nutrition, rather than the social, joyful event
of a meal shared. It became so tedious and difficult that it simply
wasn’t worth going out. I hated to make a fuss. I had been that
person who would eat anything, anywhere. I was a foodie. Now
I had to be that challenging woman who seemed to make a fuss
out of the simple act of ordering from a server! I hated being that
woman. To this day, Erin still apologizes as she asks for servers
to make special accommodations for her order at a restaurant.

I learned that food defines us. Take away one of the major
food groups and you change a person forever. Few other dietary
restrictions would cause such an emotional impact. For example,
take away vegetables, and you end up with a person who is less
healthy, but not mournful. Take away breads, cakes, etc., and
you end up momentarily with an emotionally altered person.
But, you also save a life or, at the very least, improve the quality
of life and health. It is well worth the trade!

ACTIONS

Being the determined women we are, we simply read how
to ferret out the hidden sources of gluten, and we stopped
eating it. All together. All at once. And we never looked back.
We read labels and we read labels and we read more labels.
The positive impact, or should I say, the incredible cessation of
sickness that we had all accepted as “normal,” was so sud-
then that not one of us even thought about eating it again.
Okay, I may have had two individual pieces of pizza on two
occasions within the next 3 years, but on each occasion the
impact was so severe and so immediate (threw up both times within 15 minutes!) that I have not done it since. And to my knowledge, the girls have never intentionally eaten gluten since we stopped in February 2007.

Early on, I tried a gluten-free hamburger bun. It was shelf-stable for a year! It was made almost exclusively with white starches and white rice and was full of preservatives. Keep in mind that before the inclusion of preservatives and chemicals, bakeries sold day-old bread at a discount; bread was never intended to be shelf stable. The buns were so awful I simply threw them out. Like virtually everything available in 2007, they were highly processed carbohydrates: awful, empty, bad-for-your-body-in-every-way carbs. I wasn’t going to eat a food that was dry, crumbly, tasted like cardboard, and had absolutely no positive nutritional value. So, we simply didn’t eat baked goods in any form. We all ate sweet potatoes, beans, salads, meats, fruits, and vegetables. In the beginning, for Erin and me, the potatoes and beans were important as our bodies learned to live with a new and healthier form of carbohydrates. Taylor had long ago adjusted to a life without bread. Our experience showed us the need for our gluten-free—turned allergen-free bakery.

THE BAKERY
Learning to bake again

Mom made everything from scratch. And she taught me to bake, as her mom taught her and her grandmother taught her mother. I passed it on to my kids, with a touch of “organic” already seeping into our food. As early as 1976, my sister called me a “granola head” and asked me why I was attempting to make a whole-wheat, carob chip cookie. Clearly, I always believed there had to be a way to eat “comfort food”—food that simply made you smile by eating it or thinking about the memories surrounding it—without having to pay an inherently horrible price with your body. What we eat definitely impacts our long-term health: we truly are what we eat!

I was so sad and so lost that for the first year I didn’t even try to bake. Two holidays came and went. Taylor had begun playing with gluten-free granola bars. In the summer of 2009, she came up with one that was so great and nutritionally balanced that she called it a FoodBar. She is talented and clever. She figured out how to package it and seal it and even designed and produced a label for it. She gave it as a gift to overnight guests for her wedding. I was so proud of her, but a bit envious. I was like, “Well, if you can do that, then I can bake!” I had tried a few things in the previous 6 months from the collection of gluten-free cookbooks that were currently adorning my counters. The foods were awful. They landed in the trash. I was discouraged, but Taylor’s determination and fantastic success spurred me on.

I had the realization that perhaps these were simply bad recipes. I had spent a lifetime borrowing great recipes or being thrilled to find one good one in a cookbook. Surely it was possible to come up with soft, tasty, healthy gluten-free breads that simply tasted like good food, as opposed to good-for-gluten-free food. My inquisitive mind delved yet again into research—this time, gluten-free flours. I read and read about the various gluten-free flours and about the binders that were the essential ingredient in order to recreate the “magic” that gluten provides. (Gluten acts like a glue; it binds the ingredients together. In order to bake without gluten, a “binding” agent needs to be added. Gluten-free baking will never have the exact same texture as baking with wheat, but we have learned how to get pretty close.) After understanding the science behind baking without gluten, I proceeded. I had an old casserole bread recipe that I thought might work well with these new flours. I was right. It was fantastic, with perfect taste and texture! First the rolls worked. Then I tweaked the recipe a bit more and was able to make the round casserole loaf. Six months or so later, I was finally able to make this wonderfully old-fashioned-tasting bread into a sandwich loaf. It was an arduous journey of patience, frustration, failure, and finally success.

A perfect storm

We were a perfect storm of talents and experience, need and desire, and finally, incredible determination and perseverance. And, we had great family support and role models. Taylor’s husband is an entrepreneur: he has started three medically based businesses. He has been a wonderful inspiration, not to mention fantastic cheerleader as well as a man willing to help us in any and every way. And, I came from a long line of self-employed men. My dad had owned multiple restaurants for 44 years. Taylor and I had grown up working in them and had been a part of long-range planning. We both had business degrees from college—mine was in economics; Taylor’s was in accounting, finance, and management. I had the love of baking, I understood the essence and art and science of baking, Taylor understood how to eliminate the dairy, and she learned how to eliminate the eggs as we proceeded. Taylor had an exceptional understanding of nutrition. She is constantly reading about food and nutrition. And, most importantly, we were gluten-free.

We both quit our jobs in 2009, in the height of the worst economy since the Great Depression. We spent 6 months adapting old family favorites and learning how to go from home baking to commercial baking. We taught ourselves the various parts of a commercial business: packaging, labeling, food costs, and nutrition information per serving, not to mention the legal and administrative process of setting up a corporation. We designed our commercial kitchen and researched everything from the best ingredients to the proper equipment. It was a huge task.

Principles and expansion

Our bakery began with the basic principle of being 100% gluten-free while being as healthy as possible. We were negating the impact on our bodies of our modern diet: a diet full of preservatives, highly refined and genetically modified ingredients, and overuse of sugar, fats, and salt. We reduced the sugar, used only heart-healthy fats, and used organic ingredients where it was feasible. Over the past 3 years, the bakery has turned into so much more due to customer requests as well an increased understanding of the incredible severity and impact of food allergies. Immediately we became soy-free and decided to remain as dairy-free as possible. Within the first 6 months, we took the
corn out of all but four products, two of which were cornbread. After 18 months, we reduced the sugar in all of our yeast breads by 50%, and we offered some tapioca-free breads, a line of anti-Candida (yeast-free, sugar-free) breads, and a paleo line of products free of grains, sugar, dairy, and legumes. Nineteen items turned into 160 or so! If it is a chemical/preservative or an allergen that makes people sick, we can and do keep it out. We couldn’t be more proud of the range and quality of bread products that we have developed to serve the varying needs of our customers. Our referrals at this point come from word of mouth, our Facebook page, the unsolicited press that we have received, or doctors. Can you imagine doctors sending patients to a bakery?

Fast forward to 2010 and you’ll see that the Dallas Morning News titled their article about us “Building a Better Bakery.” I take that as a true compliment! Clearly, Taylor and I have always thought that food was in integral part of health, while baked food is a key to a person’s happy place. We put our thoughts into action.

Stories from inside the bakery

If the walls could talk inside our bakery, your heart would melt. Tears from mothers, or smiles from the children, as we bring some sense of normalcy back to even the sickest of our customers, are equally emotional and inspirational. If you could only hear these tales, you would feel more than blessed to have only a simple gluten allergy, or even a gluten and dairy allergy. We have babies who enter this world allergic to gluten, eggs, dairy, and soy. Consequently, their nursing mothers come to us to buy our food so their milk is acceptable for their babies. We also have children, one in particular, the 4-year-old son of an otolaryngologist, who is still suffering from incredible eczema despite years of testing and doctors and adhering to the most stringent of diets. At the age of 4, before they found us, he was still living on bottled formula. I wish you could watch that wonderful little boy eat a cupcake that is free of gluten, soy, dairy, eggs, and all chemicals and preservatives. The smile on his face, and the always-thankful love we receive from his mother, are enough to keep us moving forward to continue to develop recipes that allow the severely allergic to eat with some amount of normalcy. Or there is the 11-year-old boy who never had a birthday cake until they found us. Or the cancer patients (and the cross-fitters—those who are extremely aware of the causal relationship between diet and exercise and their health) who come to eat our most specialized products: the paleo, which is free of grains, dairy, sugar, and legumes. It is anti-inflammatory and ultra-low carb. It is incredibly nutritious given it is made from eggs, nuts, seeds, and fruit.

Some of our customers can eat only our most limited breads: the anti-Candida, which is truly allergen free, with no gluten, soy, dairy, eggs, nuts, yeast, or sugar. It has been a god-send to these people, many of whom are autistic, who eat this bread. It has the taste and texture of bread, which is so important for autistic children. Autoimmune disorders are no stranger to us at Unrefined Bakery: there is a huge correlation. We have never done a scientific study, but we have more than a few with lupus, Sjogren’s, Hashimoto’s/Graves’, multiple sclerosis, muscular dystrophy, diabetes, autism, etc. (Taylor has a thyroid condition and another family member with celiac disease has lupus.) We hear their stories. We offer a shoulder. Often we learn as well.

We have become a collection point of information; more than that, we have become a family of random people with shared experiences. We share information regarding great doctors and nutritionists. This is a safe place not only for food, but for helping a customer who has become a friend. Sadly, but realistically, some of our customers get more and more sick. But in the meantime, they continue to come to us for a cookie or cupcake or a paleo loaf. They come to us because we are one of them. We get it! We offer a safe haven with food that brings a smile!

AN OVERVIEW OF GLUTEN AND CELIAC DISEASE

The National Institutes of Health indicated that, on average, “a diagnosis of celiac disease is not made until more than a decade after symptoms begin” (1). This was clearly true for me and my daughters. According to the Celiac Support Association, 3 million Americans are undiagnosed. Untreated celiac disease increases the risk of cancer 200% to 300% and increases the risk of miscarriage 800% to 900%. Individual health care costs for untreated celiac disease are $5,000 to $12,000 annually—a total of $14.5 to $34.8 billion for the United States (2).

For those with celiac disease, gluten makes them sick. Gluten is a protein found in wheat, barley, and rye. This is the common simple explanation, but it is so much more complicated than that—it has to do with the peptides within the gluten protein, glutenin and gliadin, and how in the autoimmune form, celiac disease, the villi become damaged. The villi play the important role of absorbing nutrients from food. With damaged villi, malabsorption occurs, and the body cease to function properly. Why is it so challenging to live without? Gluten is simply everywhere. It’s in the expected offenders—breads, crackers, pastas, pastries—and in less typical places like your spice cabinet and seasoning mixes. It also hides in cosmetics and medicines. It is used as a filler and a binder/thickener in our highly processed society.

Celiac disease and nonceliac gluten sensitivity are both treated by 100% elimination of gluten from the diet. This is a bit harder than it seems. It is not like sugar, where less is definitely better. It has to be 100% elimination. This mean no crumbs from toasters or shared butter or jelly jars. It means avoiding cross-contamination inside a deep fryer at a restaurant, where french fries are fried in the same grease as the chicken strips. It means you have to learn scientific words like maltodextrin and modified food starch that are found in processed foods. You have to learn to read labels. It is hard to find all the hidden places. It takes a while. This is why our customers come in with that deer-in-the-headlight look! But, there are books and blogs and support groups and people like us who have been there, done that.

Table 1 summarizes some basic information on celiac disease (3–6). Although I am not a medical expert, I continue to study this disease and found the following points interesting.
History and increasing prevalence

For humans’ first 2+ million years, we were hunters and gatherers. Our gut developed with a specific diet. Then, somewhere around 10,000 to 15,000 years ago, our lifestyle and diet evolved: we began to grow wheat and to domesticate animals. Our food changed, and so did the demands on our gut. As Dr. Stefan Guandalini noted: “The agricultural revolution of the Neolithic period generated a whole battery of food antigens previously unknown to man, including protein from cow, goat, and donkey milk, as well as birds’ eggs and cereals. Most individuals were able to adapt. Among those who could not, food intolerances appeared and celiac disease was born” (7). Although it would seem that gluten is “suddenly” on the scene, it was first documented in 200 AD by Aretaeus of Cappadocia, who wrote about “The Coeliac Affection.” Dr. Guandalini noted that Aretaeus “named it ‘koiliakos’ after the Greek word ‘koelia’ (abdomen). His description: ‘If the stomach be irretentive of the food and if it pass through undigested and crude, and nothing ascends into the body, we

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*Source: UpToDate articles on celiac disease (3–6).
call such persons coeliacs” (7). It was another 1600 or so years, the late 1880s, before modern science began delving more deeply into the correlation between our gut and what we put into it.

It seems clear—from the labeling of products on supermarket aisles, to magazine and newspaper articles, to the latest professional athlete seeking to find an edge—that gluten is on the brain and on the rise. An article from the Mayo Clinic summarizes current thought based on interviews with Joseph Murray, MD:

Mayo Clinic research suggests the disease is becoming a major public health issue. Although the cause is unknown, celiac disease is four times more common now than 60 years ago, and affects about one in 100 people. According to Mayo studies, undiagnosed celiac disease can quadruple the risk of death. Mayo researchers are working to discover the causes and improve diagnosis. Their effort . . . tells us that whatever has happened with celiac disease has happened since 1950,” Dr. Murray says. “This increase has affected young and old people. It suggests something has happened in a pervasive fashion from the environmental perspective.” . . . Mayo researchers learned that those whose gluten intolerance had not been diagnosed in the 1950s were four times likelier to have died. “Having undiagnosed celiac disease is not good for you,” Dr. Murray says. “It may take 20 to 30 years for that risk to become apparent. But there’s a good chance it’s a problem.” . . . About one-third of the population carries the genetic background for gluten intolerance—but only 1% of people have it. Before causes can be tested in the lab, researchers must develop an animal model with celiac disease.

Dr. Murray lists several possible environmental causes of celiac disease. The “hygiene hypothesis” suggests the modern environment is so clean that the immune system has little to attack and turns on itself. Another potential culprit is the 21st century diet. Although overall wheat consumption hasn’t increased, the ways wheat is processed and eaten have changed dramatically. “Many of the processed foods we eat were not in existence 50 years ago,” Dr. Murray says. Modern wheat also differs from older strains because of hybridization. Dr. Murray’s team hopes someday to collaborate with researchers on growing archival or legacy wheat, so it can be compared to modern strains (8).

Again, these views are not hard to find, or to believe, but as a layman, it is simply better to put in the views of a highly qualified health professional.

Obtaining a diagnosis

As indicated by The University of Chicago Celiac Disease Center (9), it can be useful for patients to be tested for celiac disease and have an official diagnosis rather than just attempting a gluten-free diet, as Taylor and I did. The term “gluten intolerance” is used when discussing the whole spectrum of conditions associated with gluten-related illnesses. The different conditions—celiac disease, nonceliac gluten sensitivity, wheat allergy, sensitivity to foods rich in FODMAP (fermentable oligosaccharides, disaccharides, monosaccharides, and polyols)—have differing mechanisms of action, severity of damage, and complications. “Plus, autoimmune diseases tend to cluster together in one individual and celiac disease is an inherited disease, so we believe it wise to understand the health risks for your other family members” (9).

Coexisting sensitivities and food allergies

As Vikki Petersen, DC, CCN, indicated, gluten-sensitive patients often don’t tolerate dairy products. She listed three main reasons: enzymes, allergens, and morphines (10). The Celiac Disease Center noted, “It’s possible to be intolerant to other substances as well as gluten, but intolerance for one does not necessarily cause or occur with the other more frequently. Many who have celiac disease are also lactose intolerant, but it often resolves after the gut has a chance to heal” (11).

Awareness of food allergies has been important in our bakery. The top food allergies, which account for about 90% of allergic reactions, are milk, eggs, peanuts, tree nuts (almonds, cashews, walnuts), fish, shellfish (such as crab, lobster, shrimp), soy, and wheat (12). According to Food Allergy Research and Education:

Researchers estimate that up to 15 million Americans have food allergies. This potentially deadly disease affects 1 in every 13 children (under 18 years of age) in the U.S. That’s roughly two in every classroom. The economic cost of children’s food allergies is nearly $25 billion per year. According to a study released in 2013 by the Centers for Disease Control and Prevention, food allergies among children increased approximately 50% between 1997 and 2011. The number of people who have a food allergy is growing, but there is no clear answer as to why (13).

Gluten and neurological symptoms

The bestselling book Grain Brain (14) has brought public awareness to the impact of grains, gluten, and sugar on inflammation and its long-term effect on the human body. The author, David Perlmutter, MD, stated his argument in the introduction to his book:

I believe that the shift in our diet that has occurred over the past century—from high-fat, low carb to today’s low-fat, high-carb diet, fundamentally consisting of grains and other damaging carbohydrates—is the origin of many of our modern scourges linked to the brain, including chronic headaches, insomnia, anxiety, depression, epilepsy, movement disorders, schizophrenia, attention deficit hyperactivity disorder (ADHD), and those senior moments [including Alzheimer’s]. (14).

He related the link to inflammation: “All of the neurodegenerative diseases are really predicated on inflammation” (15).

Dr. Perlmutter calls himself the Empowering Neurologist. I have learned through my own experience and the experiences of my family and customers that there is indeed power in changing what we eat and watching our health reappear.

Dr. James Hamblin, medical editor for The Atlantic, interviewed Dr. Perlmutter for his article, “This is Your Brain on Gluten” (15). Dr. Hamblin expressed skepticism that any one factor can be the end-all, be-all, cure-all to neurologic disease. In his explanation, Dr. Perlmutter commented:

People say “What you’re promoting here is really outside the box. Is that your mission?” I try to explain that, no, my mission
is to make this inside the box. To make the box bigger. So that mainstream medical professionals will begin to discuss the importance of these factors. Because it’s already there. In the peer-reviewed literature. It’s been there for decades. There’s nothing proprietary about this. Every peer-reviewed article is available in the “Science” section of my website (15).

The idea of medicine being integrative was once implicit. Why is it thought of as “outside the box” or alternative for people to look at the totality of their diet, exercise, and/or stress as possible factors in their overall health? How did we ever think that what we eat or drink or how we do or do not exercise wouldn’t impact our long-term health?

Hamblin’s article also quoted Dr. Perlmutter on gluten insensitivity’s wide-ranging effects, of which all physicians need to be aware:

The gastroenterologists don’t seem to realize that gluten insensitivity far exceeds their area of focus. According to the work of Dr. Marios Hadjivassiliou in England, there are a large number of people who have reactions to gluten that have absolutely nothing to do with the gastroenterologist. Manifestations can occur anywhere in the body. The work of Dr. Alessio Fasano at Harvard indicates that perhaps all humans have some negative reaction to gluten. Gluten induces this cornerstone of brain degeneration: inflammation. It causes leakiness of the blood-brain barrier (15).

This passage from the Journal of Gastroenterology and Hepatology also speaks to the impact of gluten on the brain:

Neurologic manifestations are among the most common extraintestinal features of celiac disease. . . . While celiac disease continues to be underdiagnosed in the West, a low index of suspicion among physicians in the developing world has led to gross under-recognition of the disease elsewhere. Celiac disease can affect multiple organ systems, and its tremendously varied clinical presentation implies that physicians of all specialties should keep this condition in mind when evaluating patients (16).

MY WORDS, MY BELIEFS, MY SUMMARY

I know so many readers have their own story, their own frustrations and losses. To you I ask: please listen and know that my success was confirmed long before we opened our bakery. It was nearly immediately apparent when I made the conscious decision to stop eating gluten. As Erin said after finding out she had celiac disease, “Nothing tastes as good as feeling healthy.” A wonderful side effect of going gluten-free was awareness of nutrition labels. I realized the “junk” that is actually in the food of a typical 21st-century American diet. My diet gradually morphed into being cleaner and more organic.

Those with gluten intolerance need to be their own advocates. Read and research. Teach yourself. Even teach your doctors. Don’t take no for an answer. Don’t be afraid of losing the gluten. Life without it is a great life. Health is priceless—so much better than a slice of pizza or a cinnamon roll (my two weak spots).

Doctors, please listen to your patients. The scope and variety of symptoms are so expansive, so seemingly random and unrelated that a person can feel a bit crazy when trying to put them all together. I ask you to be the one who helps your patients find the answers they so badly need. Please help us help ourselves. The science behind the various foods that we eat will be left for the researchers and scientists to ultimately discern. I predict it will be a long time before we have answers. Perhaps, as with all medicine, the “answers” might still be the best guess with the best intention after correlating the best research from the brightest minds.

My philosophy that carried us through these huge changes is this simple: Life works in mysterious ways. For me, I have found that life is what it is: I take the “givens” that land in my lap; I learn as I go; I focus on the positive; I share my gifts and talents. My daughters seem to do this too. We three have learned that these “bumps” can be the best thing ever. It is part of what makes us unique. Living gluten-free has brought us the gift of health.

15. Hamblin J. This is your brain on gluten. The Atlantic, December 2013. Available at http://www.theatlantic.com/health/archive/2013/12/this-is-your-brain-on-gluten/282550/.
Salt Sugar Fat: How the Food Giants Hooked Us by Michael Moss


Reviewed by John M. Pogue, MD

In grocery stores and supermarkets, food sections may be roughly divided into two categories: (A) fresh produce, and (B) processed, prepared, preserved, and packaged food. The foods in category A, the vegetables and fruits of the produce section, promote heart and general health. Unfortunately, the foods in category B, processed foods, are today preponderant in the American diet. Is it a coincidence that obesity is widespread?

By a vote on June 18, 2013, the delegates at the annual meeting of the American Medical Association classified obesity as an official disease. In 2004, the US Department of Health and Human Services designated obesity as a disease. In 1998, the National Institutes of Health declared obesity a disease, and the US Surgeon General, David Satcher, MD, pronounced obesity a “national epidemic” as well. At least on one occasion in the 1990s, the US Surgeon General of the Department of Health and Human Services, emphasized that since 1993 the Food and Drug Administration had identified 60,000 processed food products in supermarkets (pp. 27, 98), relying on salt, sugar, and fat, which “override our dietary self-control” with foods “so perfectly engineered to compel overconsumption” (pp. xix, 253, 333, 346). Salt, sugar, and fat are “the three pillars of processed food” (pp. xii, 22, 39, 70, 264, 281, 289, 293, 337). With sugar and fat intake, brain pleasure centers light up bright yellow in functional magnetic resonance imaging studies (pp. 148–149, 276), just as with cocaine (pp. xxvii). Increasing the amount of sugar intake leads to a “bliss point” (a range) of maximum taste satisfaction, disposing the consumer to crave sugar (pp. xxvi, 10, 11, 30, 34, 38, 42–43, 316) in a virtual addiction. This causation of the National Institutes of Health’s Nora D. Volkow, MD, to urge some people to “just stay away” from processed sugar (p. 342). On average, Americans consume 22 teaspoons of added sugar per day (pp. 4, 23, 362n4), over two-thirds from processed food (p. 17). A 20-ounce soda has 15 teaspoons of sugar (p. 99). (One teaspoon contains 4.2 g of sugar [p. 370n59].) The American Heart Association suggests a limit (beyond needs) of five teaspoons per day for women and nine for men (p. 23). Nearly all processed food has added sugar, including high-fructose corn syrup (p. 21). Excess sugar intake is stored as fat (pp. 31, 116). Newborn babies love sugar (pp. 11, 18). Babies dislike salt, but adjust to liking it, upon coaxing, on or after the age of 6 months; the food industry has created a craving for salt (pp. 10–11, 278–280).

Increased saturated fat intake correlates with obesity and type 2 diabetes and with “cholesterol, clogged arteries, heart attacks, and strokes” (pp. 187, 214–215). Michael Moss stresses that “fat is an energy colossus. It packs 9 calories into each gram, more than twice the caloric load of either sugar or protein” (pp. 153, 263–264). For fat, instead of a “bliss point,” there is a quite potent “mouthfeel” (dryness, gumminess, and moisture release); in terms of its allure, fat can be added to food without limit (pp. 42, 154, 157–158, 171, 174, 218, 264, 329). Cheese is the biggest single source of saturated fat, which is converted by the liver into cholesterol (p. 163). Besides cheese, sources of saturated fat include pizza, red meat, chocolate cake, cookies, frozen dinners, candy, potato chips, corn chips, butter, and mayonnaise (pp. 178, 213, 215–216). The US Department of Agriculture’s recommended daily limit for saturated fat is 15.6 g (pp. 155, 215).

Caldwell B. Esselstyn Jr., MD, a former Cleveland Clinic surgeon and the present director of the Cardiovascular Prevention and Reversal Program at the Cleveland Clinic Wellness Institute, emphasized that since 1993 the Food and Drug
Administration permits food manufacturers to label (on packages and bottles) a product “fat free” or with “zero fat” if it contains less than 0.5 g of artery-clogging fat per serving. If salt, sugar, or fat is reduced, often one or both of the other two components of this triad are increased (pp. xxvi, 70). Fierce competition exists to outsell competitors and to enhance market volume, market share, shelf space share, and stomach share (pp. xii, xiii, xxix, 26, 27–28, 48, 83, 89, 95–96, 108–109, 110, 239, 257, 262, 310, 320, 338, 340, 377n110); Wall Street analysts and shareholders press and push for profits (pp. 262, 301, 322, 338–339).

Increased salt intake over time correlates with hypertension, stroke, myocardial infarction, and kidney damage (pp. 267–268, 271, 291, 295, 302, 304, 310). In Finland, government-promoted per capita salt consumption reduction by one-third correlated with “an 80 percent decline in the number of deaths from strokes and heart disease” (pp. 302–303, 310).

In the US, the salt intake of boys in their teens and men <40 is more than 10,000 mg per day (p. 268). Table salt contains 40% sodium; 10,000 mg of salt contains 4000 mg of sodium (p. 403n268). The federal government’s suggested limit is 2300 mg of sodium a day (1500 mg for those particularly vulnerable) (pp. 271, 282, 290, 404n271). (One teaspoon of salt has about 6000 mg of salt, i.e., 2300 mg of sodium [p. 403n268].) The American Heart Association advises all adults to consume <1500 mg of sodium a day (p. 404n271).

Three-fourths of salt intake is from processed foods (p. 270), with only 6% of sodium intake from table salt (p. 269). Almost all processed food has added salt (p. 270). Salt has “addictive qualities” (pp. 276–277, 283, 305).

A weighty, grave indictment of processed foods, those foods that have great amounts of salt, sugar, and fat added, arises from the fact that many leading executives in the processed food industry with vigilance and diligence avoid eating the products of their own companies (pp. xvi–xvii, 39, 123, 208–209, 250–251, 314, 336, 341).

Long ago, American women generally were homemakers, preparing meals from scratch using fresh foods (pp. 61–66). Today, about 80% of women aged 25 to 54 are in the workforce (p. 246), and many have never been taught how to “cook from scratch” (pp. 64–65, 220). Americans largely depend upon processed foods (with much added salt, sugar, and fat—preservatives, maskers of poor taste, and crave-creators) sold in grocery and “convenience” stores and in supermarkets (pp. xiii, xxix, 38, 57, 210, 220, 270, 283, 288, 300). A land of fresh food has become a land of factory food and fast food—and a land of fatness, of overweight and obese people, including children. The corporate food factories are consistently in control of culinary cooking culture (and of consumer cravings). Combined with limitations on salt, sugar, and fat, cooking from scratch switches control to the consumer. Long live this empowerment!

The reviewer, John M. Pogue, MD, is a member of numerous cardiology societies in North America and Europe, including Great Britain—where he is an elected member of the British Cardiovascular Society.

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Almost 60 years ago, I was a freshman at Davidson College in South Carolina. Occasionally, I would go to the college library but would procrastinate by perusing a list of the annual valedictorians and presidents of the student body. These lists were located on a wooden plaque next to the door of the library. The names each year were different—except in 1943, when Myron G. Sandifer Jr. filled both positions. My mother later told me that Myron was a cousin on my father’s side and that my father was an usher at his father’s wedding in Chester, North Carolina, which was 7 miles from Myron’s home in Lowrys, South Carolina. (I also found that his father, Myron Sandifer Sr., was a pallbearer at my grandfather’s funeral in Chester.) A few years later I was a senior at my social fraternity, Kappa Alpha, and was briefly introduced to Myron Sandifer Jr., who was there for his 15th reunion at Davidson and was a physician at the University of North Carolina after graduating from Harvard Medical School.

For the next 56 years, I did not think about Myron until I started remembering his name, thinking of Davidson College. From the Davidson archivist, Jan Blodgett, I received his information and was told that Davidson did not realize that he was the only alumnus simultaneously valedictorian and student body president. I also received information on Sandifer from my cousin Leila Welch from Birmingham and my cousin Bill Marion, an attorney from Chester, South Carolina. Finally, Dr. Myron G. Sandifer Jr.’s son, Myron “Mike” G. Sandifer III from Washington, DC, was significantly helpful in adding numerous stories of his father and their visits in Chester and Lowrys, SC, when he was a teenager. When I talked to Mike about his father’s receiving both honors in 1943, he said that his father was very humble and didn’t boast about it to the rest of the family. Mike said that the reason his father was so brilliant was that his mother had urged him to read at age 3, especially the book *King Arthur and the Round Table*.

Myron Jr. grew up in the small hamlet of Lowrys (population of about 100), which was 7 miles northwest of Chester, on the borderline between Chester and York counties. His school had only two rooms through the seventh grade, after which he attended Chester High School. In Chester, one of his closest friends was George Gregory Jr. (1921–2001), born in McConnells, SC, who was in the class of 1939 at Chester High

### Table. Key events in the life of Myron Guy Sandifer Jr., MD

<table>
<thead>
<tr>
<th>Event</th>
<th>Location/description</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>Lowrys, SC</td>
<td>1922</td>
</tr>
<tr>
<td>Education</td>
<td>Chester High School, Chester, SC (president of class, sophomore, junior, and senior)</td>
<td>Graduated 1939</td>
</tr>
<tr>
<td></td>
<td>BS: Davidson College</td>
<td>1943</td>
</tr>
<tr>
<td></td>
<td>MD: Harvard Medical School</td>
<td>1947</td>
</tr>
<tr>
<td>Residency</td>
<td>Medicine: Massachusetts General Hospital</td>
<td>1947–1949</td>
</tr>
<tr>
<td></td>
<td>Psychiatry: Yale University Medical School</td>
<td>1949–1950</td>
</tr>
<tr>
<td>Service</td>
<td>US Navy</td>
<td>1950–1952</td>
</tr>
<tr>
<td>Fellowship</td>
<td>Psychiatry: Beth Israel Hospital, Boston; Massachusetts Institute of Technology, Cambridge</td>
<td>1952–1955</td>
</tr>
<tr>
<td>Teaching appointments</td>
<td>University of North Carolina School of Medicine: Associate professor</td>
<td>1955–1965</td>
</tr>
<tr>
<td></td>
<td>Columbia University: Clinical professor</td>
<td>1965–1966</td>
</tr>
<tr>
<td></td>
<td>University of Kentucky: Professor of psychiatry</td>
<td>1966–1968</td>
</tr>
<tr>
<td></td>
<td>Acting chairman</td>
<td>1968–1969</td>
</tr>
<tr>
<td></td>
<td>Associate dean for academic affairs</td>
<td>1969–1975</td>
</tr>
<tr>
<td></td>
<td>Professor of family practice</td>
<td>1974</td>
</tr>
<tr>
<td>Certification</td>
<td>American Board of Psychiatry and Neurology</td>
<td>1954</td>
</tr>
<tr>
<td></td>
<td>American Board of Internal Medicine</td>
<td>1974</td>
</tr>
<tr>
<td>Honors</td>
<td>Outstanding junior cadet, ROTC battalion</td>
<td>Davidson College: Phi Beta Kappa, Omicron Delta Kappa, valedictorian, president of student body, president of social fraternity (Kappa Alpha), permanent class president</td>
</tr>
<tr>
<td></td>
<td>Harvard Medical School: senior class president, permanent class president</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>Age 81</td>
<td>Sep 2003</td>
</tr>
</tbody>
</table>

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George was also president of the student body as an undergraduate and law student at the University of South Carolina. After working as a lawyer and judge in Chester, George became chief justice of the South Carolina Supreme Court. Despite his personal disability of polio in childhood, Justice Gregory was an avid sports enthusiast and had near-perfect attendance at USC football and basketball games. He and Myron played golf and together won the horseshoes championship of Chester County! George and Myron were great friends, and both had outstanding careers. Mike spent many hours in his teens visiting the families of the Gregories and also other families in Chester, Lowrys, and McConnells, including the Wilsons, Guys, Darbys, Loves, and Williams.

Myron’s older brother, Dr. S. Hope Sandifer, was a graduate of The Citadel and the Medical College of South Carolina. He practiced cardiology and was a professor at the medical college in Charleston, spending years in research. Myron’s maternal grandfather was Rev. Samuel Rainey Hope (1859–1943), who graduated from Davidson College in 1882 and also from Princeton University in theology and was a missionary in Japan for 15 years.

Myron Jr. loved Davidson College and had several friends and colleagues there: Sam Spencer (who graduated in 1940 as student body president and salutatorian and was later president of Davidson College), C. Shaw Smith (who was in charge of the union and student activities), and Chalmers Davidson (who was from Chester and was an author, historian, professor, and chief librarian at Davidson).

Mike sent two letters from 1942 from Davidson College, one written by a freshman from Chester, Heyward McDonald, to his high school math teacher, Maud Bigham, describing Myron Jr. as a “Chester County boy who’s made good in a big way. . . . He’s never too busy to talk to you for 2 or 3 minutes and he’s a wonderful influence.” The second letter was penned by Myron Jr. to Miss Bigham in March 1942 to thank her for her letter, commenting that he would try to visit her over spring vacation.

During World War II, Myron Jr. was deferred at Davidson by achieving a research fellowship for his medical education and residency. He later served in the US Navy in the Korean War from 1950 to 1952, especially working on “post-traumatic stress disorder.” Mike pointed out that his father was a good teacher in medicine and was an expert on schizophrenia, respected by all of his colleagues and patients. He was certainly an outstanding man and provided great service in his field. He was beloved by all and was a born leader.
Environmental cleaning behavior: embedding and spreading best practice

Ramphal et al are to be congratulated for their study into the effect of their intervention to improve hospital staff compliance with environmental cleaning behavior (1). They should also be congratulated on the results: a clear improvement in cleaning behavior. As the authors admit, there is no absolute guarantee that the intervention caused the fall in the number of infections; however, improved cleaning is likely to have had at least some effect.

Despite the success, it is still worth considering how the quality improvement project could have been run even better. The investigators measured at regular intervals, but they might have had even better results by measuring continuously (2). A continuous measurement and feedback process with real-time feedback might have resulted in even greater improvement. It also might have motivated all staff to consider how they could further “improve” their improvement intervention. Staff on the ground might find that certain methods work better than others and could have learned in the process and improved even more as a result.

The quality improvement intervention was trialed on the medical and surgical wards and was undoubtedly a success by the end of the project. However, the authors could have mentioned whether they planned to embed the new improved cleaning behavior in standard processes and ensure that it became part of the standard of care on those wards in the future. Unfortunately, quality improvement projects all too often slip back at the end of their natural lifespan; best practice is to ensure that changes become part of the normal and permanent processes of the ward.

The best quality improvement projects also change the culture of the health care team, as all members of the team start to feel empowered to improve the care that they deliver. It would have been interesting to know whether a similar phenomenon occurred on the medical and surgical wards of this institution.

Finally, it would have been interesting to know whether the authors planned to disseminate the good practices that they had developed. The medical and surgical wards are no doubt just some of the wards in the institution, and it is likely that at least some of the other wards would have benefited from learning from the experiences of their colleagues who conducted the quality improvement project. The authors certainly had a great success and the whole institution could thus follow their lead.

—Kieran Walsh, MD
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THE AUTHORS RESPOND:

Thank you for your comments regarding our article. To respond to your queries:

Continuous intervention and measurement: We would very much have liked to have had the funds to measure the process continuously. However, since the study was not funded, we did not have the manpower to measure outcomes in real time. The intervention at the level of the environmental services (EVS) managers was continuous; however, they also lacked the manpower to measure on a daily basis.

Embedding the process into the cleaning protocols of the hospital: Changes in the cleaning process were embedded into the cleaning protocols commensurate with the unfolding of the project, which took 1½ years to finish. The hospital where this project was completed is extremely committed to the children they serve. When they detect a way that they can improve their outcomes, they implement these methods immediately.

Changing the culture of the staff: One of the best features of this project that we failed to mention is that the biggest jump in success, from 19% to 49%, occurred because we realized that many of the cleaning staff were not native to the US. We encouraged EVS to train the staff bilingually, which better highlighted the mission, the message, and the purpose of the project to the staff. Sensitivity to the culture of the staff was critical to the success of communication with the staff and ultimately to the success of changing behavior and improving outcomes.

Influencing other departments in the hospital: The EVS staff was in charge of cleaning all departments within the hospital, but not the outlying clinics. The hospital has a very aggressive handwashing teaching module that is required for all staff. This module has produced impressive (97%) handwashing rates among all staff, even in the outlying clinics. It would take some time, however, before a cleaning module could be developed and integrated into a similar module. If it were required of all EVS staff and staff in the outlying clinics, there would be a similar impact. At this time, such a teaching module does not exist.

—Lilly Ramphal, MD, MPH
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I enjoyed reading the case report by McKernan et al (1) and the accompanying editorial by Schussler (2), published in the April 2014 issue, about a 77-year-old woman who suffered Takotsubo syndrome (TTS) following a thoracic epidural steroid injection for postherpetic neuralgia. The authors and the editorialist opined appropriately that many factors, along with the procedure, had conspired for the emergence of TTS in this patient. However, what surprised me was the statement of the editorialist about the cause of TTS, that “it is becoming clearer that the final common pathophysiology pathway may be coronary spasm, although the details remain to be worked out,” citing the work by Patel et al (3). Patel et al studied the coronary vascular reactivity (both coronary epicardial and microvascular responses) of 10 women at a median of 5 months after an episode of TTS, employing intracoronary infusions of acetylcholine, nitroglycerine, and adenocine, and measured the percent change in coronary vessel diameter and in coronary blood flow. The authors found in their patients mild epicardial vasoconstriction, and markedly decreased coronary blood flow reserve, in comparison with a reference cohort of 211 women from their laboratory (3). Although Patel et al documented severe, primarily microcircular, impairment in these 10 patients with prior TTS, which conceivably "may be a central feature of the pathophysiology of TTS," they added that "since the coronary physiological assessment was performed after the episode of TTS, we cannot be certain as to whether the abnormality on coronary vasomotion detected was present prior to the onset of the cardiomypathy." Considering that many myocardial derangements (e.g., myocardial edema and electrocardiogram QTc interval prolongation) persist long after the normalization of the left ventricular function after a bout of TTS, it is imperative that an assessment of the epicardial vessel and microcirculation function be carried out many more months after full recovery of patients after TTS. Otherwise, what was found by Patel et al (3) may not be the cause, but the consequence (epiphenomenon), a lingering effect of the affliction. Indeed, one could go further to speculate that even chronic microcirculation dysfunction in some postmenopausal women may predispose them to TTS (facilitator), in the emergence of a pathophysiological mechanism (cause) not yet discovered.

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Kudos

The white coat lecture by Dr. Knowlan is so thoughtful. Would it be possible to get offprints of the speech to place in my waiting room? As always, I really enjoy reading the BUMC Proceedings.

—SAM MARYNICK, MD
Dallas, Texas

Editor’s note: We sent Dr. Marynick copies of this reprint and also sent copies to Georgetown, where they were distributed to all first-year medical students.
Facts and ideas from anywhere

MICROBES

Sam Kean recently reviewed two books, *The Amoeba in the Room* by Nicholas P. Money and *Missing Microbes* by Martin J. Blaser (1). Kean begins by telling how geneticist Craig Venter took a sailing trip to Bermuda and while there decided to do a little research. He hauled up 50 gallons of the Sargasso Sea and began trawling it for DNA. The water was cold and appeared sterile, but Venter found 1.2 million distinct genes in his sample, all new to science. Based on previous research, he knew that none of the DNA came from fish or plants or any other visible life form. It was all microbial. For perspective, human beings have 23,000 genes; Venter had uncovered perhaps thousands of new microbes without even trying.

This Bermuda experiment underlined something biologists have argued for years: that we know virtually nothing about the world of microbes. By every fair reckoning, viruses, bacteria, and other one-celled organisms dominate life on Earth. Bacteria outnumber all plants and animals by several orders of magnitude, and viruses outnumber bacteria. Microbes also outweigh people. Just the bacteria found in the ocean weigh more than all the elephants on Earth—millions of times more. Yet, we have not even been able to grow most microbes in the lab to study them.

In *The Amoeba in the Room*, Money, a mycologist at Miami University in Ohio, deploys several strategies to enlarge our appreciation of the microscopic. He indicates that “a pinch of soil may seem inert but it contains 1 billion bacteria and tens of millions of fungi and protists. Ten thousand bacteria could be squeezed inside the period at the end of this sentence, and one gram of pure bacteria contains 2 trillion cells.” And microbes are tough. Some species live in the pH equivalent of battery acid, while others prefer bleach. Some live at depths of 36,000 feet in the Pacific Ocean; others waft miles above the atmosphere. Some have colonized Chernobyl.

*Missing Microbes*, by Martin Blaser, an infectious disease specialist at New York University, focuses on a profound concern: the damage that modern life inflicts on the vast number of microbes that all of us, even healthy people, carry inside us at all times. A human being consists of 30 trillion cells but 100 trillion microbes, and they colonize every niche inside us. We are conditioned to think of microbes as dirty parasites. Most microbes, however, are harmless, and many perform vital metabolic functions. Some digest carbohydrates; others help absorb nutrients like salt and water. Some regulate our blood sugar and still others manufacture vitamin K. We would die without these microbial partners, and at some point the distinction between “us” and “them” becomes meaningless. Blaser compares this “microbiome” to a full-fledged internal organ—one that weighs 3 pounds, as much as a human brain. And just like a kidney or liver, a microbiome can fail.

Blaser describes a vivid anecdote involving his daughter. While an infant, she suffered from ear infections and was given strong antibiotics. Over the next few years she developed mild asthma and a mango allergy. In her teens and 20s, she began traveling widely in Latin America where she inevitably battled diarrhea. Another course of antibiotics cleared it up, but she soon began suffering from chronic stomach pains. Several years of misery later, a specialist finally diagnosed celiac disease—even though she had never had trouble eating gluten before.

Although it may have been a coincidence that his daughter’s asthma and her food allergies both first appeared after she took antibiotics, Blaser suspects otherwise. He argues that while effective in clearing up her acute infections, the drugs also caused collateral damage, wiping out essential microbes and somehow inducing these chronic conditions. He doesn’t limit himself to these elements either. He blames the rise of autism, juvenile diabetes, obesity, and Crohn’s disease—each of which have skyrocketed in recent decades—on missing microbes.

Although to a person with a microscope, every disease looks microbial, research does lend some support. Mouse studies have linked disruptions in the microbiome to a number of medical scourges, including obesity. And modern medicine, as well as factory farming, exposes us to more and more powerful antibiotics. Because antibiotics are blunt, killing friend and foe alike, prescribing strong doses to children might well disturb the establishment of a proper microbiome early in life. A rise in Caesarean sections also cheats a newborn of exposure to a mother’s vagina, which houses several essential microbes.
When it comes to microbes, our ignorance runs deep: we barely know what we don't know. Both *Missing Microbes* and *The Amoeba in the Room*, for all their differences, lay out the disturbing consequences of that fact. As one microbe researcher has put it: “I make no apologies for putting microorganisms on a pedestal above all other living things. . . . Killing all certain species of microbes would spell doom for us and perhaps the whole planet.”

**PATH TO HAPPINESS**

Hugh Hewitt has just published *The Happiest Life*, his 15th book (2). Hewitt is a renaissance man, the host of a nationally syndicated coast-to-coast show called the *Hugh Hewitt Show*, Monday through Friday from 6:00 to 9:00 PM Eastern. He also is a professor of law and a lawyer in private practice. He writes weekly for the *Washington Examiner* and www.TownHall.com and lectures frequently at colleges and universities. In his radio and television activities, he has interviewed far more than 10,000 people, perhaps double that number, and, therefore, has acquainted himself with numerous points of view.

His latest book describes the seven gifts for happiness and the characteristics of the seven givers. The seven gifts he describes are encouragement, energy, enthusiasm, empathy, good humor, graciousness, and gratitude. Each is preceded, he cautions, by generosity. He also uses the phrase “for the most part,” indicating that nobody gets out of here without pain or sorrow along the way. Hardship and grief, he emphasizes, are inevitable in all of our lives and are crucial to the happiness that the seven gifts he discusses make possible.

Hewitt obviously has talked to a number of friends and interviewees about happiness and the path to happiness. Interestingly, money is not discussed at all. One of his interviewees, citing numerous studies by the best academics in the world, argued that having at least two or three of the big four—namely, faith, family, community, and fulfilling work—was usually enough, but having all four increases the odds of happiness.

And bad things still happen to good people; illness and accident, of course, can upset even the happiest of lives. Hewitt argues to sacrifice everything for family, and not just immediate family but the extended family. Keep them close, he advises; spend time with them. Always put them first.

Friends matter a lot, and we should value and serve them. Seek new ones and cling to old ones. Work alongside them for the good of the community. Do not betray them or neglect them. And find something to do that you enjoy doing, adjusting your consumption to your income so that you can do work that gives you pleasure and fulfillment. All these things, he concludes, add up to “earned success,” and earned success is the essential ingredient of happiness.

He recommends watching out for the period in life that men and women are most likely to be unhappy. For men, the unhappiest period is at the age of 45, and not because of dropping testosterone levels. At that age, men realize they may have missed the “off ramp” to happiness. They may have driven past the chance for family, for deep friendship, for the sort of work that saw them spring up in the morning eager to begin a new day, and for a real relationship with God. Of course, this age thing may be a false premise, because many people find faith or friends, renewed family bonds, or a new career after age 45, but it is harder to do because of previous choices.

Hewitt also stresses that human happiness is inextricably bound with doing good. Because we are born with a conscience, actions opposite that produce profound unhappiness. The best way to achieve happiness is to do good for others—starting with the seven gifts. The best guarantee of deep unhappiness is to do injury. In truth, all one has to do to ensure misery is to be stingy with the seven gifts. The other most common destroyer of happiness is addiction.

Doing good, he emphasizes, means sometimes doing very hard things, as soldiers do in combat or police do in their work. But even the hardest things, he argues, can bring satisfaction and deep happiness if done rightly for the right reasons. Hewitt explains that he has known many soldiers, sailors, airmen, and Marines. Among them are some of the happiest, most fulfilled people he has ever met. Thiers are lives of high honor and incredible sacrifice, and they have often given more than any civilian can even imagine and seen suffering on a scale that would stun the most cynical man or woman. Hewitt also argues that living in the midst of great sacrifice and incredible suffering for the longest period of time is what made George Washington and Abraham Lincoln our greatest Americans, and is how Winston Churchill defined greatness in the 20th century. Their “earned success” was in the midst of the greatest drama possible—the fate of their entire country—but their choices came down to the same decisions every person makes about selflessness every day, earning their own success every day. Few people outside of combat have the opportunity to lay down their life for a friend, but everyone has the opportunity to give these incredible gifts.

Hugh Hewitt went to his Harvard alumni gathering 35 years after he had graduated. He asked many of his fellow reunion-goers what made them, the alumni of such an incredible institution, happy. The most common answer he received was family and friends, with faith figuring into many accounts of genuine happiness. None of those he asked mentioned money or assets. None would count material accomplishment as that which brought them happiness! These Harvard alumni represent a pretty large cross-section of people from a very diverse set of backgrounds who have pursued a great variety of careers in places all over the country and indeed the world. None of them, he emphasizes, would say that their greatest happiness came from the things they had gotten. All of them point to the people and institutions to which they had given. Hewitt concludes that “it is all about giving.”

**SOME EDWARD O. WILSON THOUGHTS**

In an interview of biologist Edward O. Wilson, the 85-year-old author of 30 books, Harvard professor of comparative zoology, and the world’s authority on ants, happiness was a topic of conversation (3). Wilson emphasized that humans are just one of 8 million species on planet Earth. He calls for an end of the “age of man,” meaning that humans should take a cautionary step back and think how we can cede more of the Earth to nature, to help stabilize the ecosystem. He worries that if we don’t, the planet.
will come to look like a spaceship run by technical geniuses. He opines that humans do not know what we are doing, that we have no goal. “You can say we want less war, or we want everybody to be happy, or we want everybody to have long lives and have good health . . . , but what kind of goal is that? That is the goal of the family dog.” He opines that what human beings really want is grace. “We want understanding, we want to be surrounded by beauty, and we want to be surprised constantly by discoveries of something unlike ourselves.” It is another reason we should leave more of the world to nature, he argues, along with “the shield that biodiversity provides us against catastrophe.” A fully functional ecosystem could help protect humans from pathogens and parasites that are kept in check by biodiversity.

Wilson's most famous book was his 1975 Sociobiology, now considered a pioneering work in the field. In his 2012 book, The Social Conquest of Earth, Wilson challenged the idea of kin selection—the long-held theory that individuals display altruistic, self-sacrificing behavior toward their relatives, with the aim of perpetuating their own genes. He put forth a theory of group selection, a kind of natural selection that acts on all members of a group rather than just related members and ultimately evolves the fitness of the entire group. I hope Dr. Wilson stays around many more years.

**RATING MARRIAGE**

Elizabeth Bernstein (4) developed a mini-test to help couples get a sense of the strength and weakness of their marriage. She developed statements for couples to answer on a scale from 1 to 5. (For the full 40-question quiz, go to www.WSJ.com/Wellness.) Sample items include the following. Trust: There is a sense of trust in my relationship. Intimacy: My partner and I have a good sex life. Validation: I listen and hear my partner; my partner listens and hears me. Conflict: When there is conflict, my partner and I can usually compromise; my partner and I are able to focus on the conflict at hand rather than bringing in other issues and escalating our disagreement. Assistance: My partner celebrates with me when something good happens to me; I celebrate with my partner when something good happens to my partner. Teamwork: My partner and I agree on financial budgeting. Boredom: My partner and I like to try new hobbies and activities together.

For couples seeking help for a troubled relationship, a rating serves as a baseline, a point from which to move upward. What does it mean when the partners’ scores don’t match? At least 25% of couples disagree on the score. In those cases the spouse who rates the marriage very low often has already mentally detached himself/herself from the relationship, while the spouse who rates it high is “totally clueless.”

Why is it so hard to clearly see and analyze the health of one’s own marriage? One reason is we don't have many role models. We don't know very much about other people’s marriages; the only one we ever see from the “inside” is our parents’. Each person brings different expectations to the partnership, and most people, even our closest friends, don't usually publicly air their marital problems, so we have no idea how our relationship stacks up next to other relationships. She advises refraining from comparing your marriage to other couples' marriages. “Evaluate your own expectations. . . . We often compare what we are getting in a relationship to what we think we should be getting. To the extent that what we are getting exceeds our expectations, we are going to be happier.”

**PLATO TODAY**

Rebecca Newberger Goldstein recently published Plato at the Googleplex (5). In the book Goldstein imagines Plato traveling on a speaking tour to places such as Google's headquarters, a cable news show, and a neuroscience laboratory. Although Plato lived >2000 years ago, his beliefs, she says, are more relevant than ever. “We are rethinking what virtue is and what it is to live a good life,” she says. For a long time, she argues, “The notion of virtue was monopolized by monotheism, by Judeo-Christian theology, but the Greeks were pre-monotheistic and they were really consumed with the question of what it is to live a life that matters. The ancient Greeks had religion but you didn’t want the attention of the Gods. They were terrible. So the Greeks approached virtue from a secular standpoint as many people do now.” Many of the questions people have today are similar to ones that came up during Plato’s time, such as whether life’s purpose is to gain fame, power, or happiness. Goldstein thinks that while our culture of self-help may sometimes stand in for religion, philosophy is much better suited to answer life’s questions.

According to Goldstein, Plato would have had strong opinions on today’s ethical questions. She believes that Plato would urge people to seek moral excellence over fame and fortune. He would also promote “flourishing,” which she describes as stepping outside oneself and learning about the world over pursuing happiness.

In the book, Plato starts his tour at Google because Goldstein thinks that tech entrepreneurs “may be the new philosopher kings.” They are the new “elite.” At first, her Plato approves of the way technology has democratized information. Then Plato realizes that everybody is going to the sources that agree with them, which she argues is dangerous for democracy. Goldstein says she now forces herself to read news from sources she disagrees with, which has helped her to change her stance on a few issues. With technology, everyone has more of a voice, but it is broadening our minds or narrowing our minds. Reading Plato convinced her of the need to be able to change her own mind, even about Plato himself. The most important lesson from Plato’s teaching, she says, is the need to look outside oneself. Your life is ever expanding the more you take in of the world. “It’s a kind of paradoxical idea that to be truly committed to yourself you have to be really committed to other things.”

Dr. Goldstein first became interested in philosophy after reading books by Bertrand Russell, Will Durant, and eventually Plato. “Reading them gave me the sense that I know nothing and I want to know something.” She soon moved on to Baruch Spinoza. “We all want to be saved one way or another whether it’s through God or philosophy or politics.” Still she thinks that philosophy can be uncomfortable. “It is supposed to shake you up,” she says. “It’s very hard for us to know the truth and when you think you know it you have to think again.”
THE DIVINE COMEDY——A SELF-HELP BOOK

Rod Dreher has characterized The Divine Comedy as a self-help book, and surprisingly that’s how Dante Alighieri himself saw it (6). In a letter to his patron, Cangrande della Scala, the poet said that the goal of his trilogy—Inferno, Purgatory, and Paradise—is “to remove those living in this life from the state of misery and lead them to the state of bliss.” The Divine Comedy does this by inviting readers to reflect on their own failings, showing them how to fix things and regain a sense of direction, and ultimately how to live and love in harmony with God and others.

The Divine Comedy arose from the rubble of Dante’s life. He had been an accomplished poet, an important civic leader in Florence at the height of that city’s powers. But he wound up on the losing side of a fierce political struggle with the pope and, in 1302, fled rather than accept a death sentence. He lost everything and spent the rest of his life as a refugee.

The comedy, which Dante wrote in exile, tells the story of his symbolic death, rebirth, and ascension to a higher state of being. It is set on Easter weekend to emphasize his allegorical connection with Christ’s story, but Dante also draws on classical sources. Dante’s masterpiece is an archetypal story of journey and heroic quest. Its message speaks to readers, whether faithful or faithless, who are searching for moral knowledge and a sense of hope and direction. In its day, the poem was a pop-culture blockbuster. Dante wrote it not in the customary Latin but in Florentine dialect to make it widely accessible. He was not writing for scholars and connoisseurs; he was writing for commoners, and it was a hit. According to historian Barbara Tuckman, “In Dante’s lifetime, his verse was chanted by blacksmiths and mule-drivers.”

Few realize the surprisingly accessible beauty of Dante’s verse in modern translation. Nor will they grasp how useful his poem can be to modern people who find themselves caught in a personal crisis from which there seems no escape. Dante’s search for deliverance propels him on a purpose-driven pilgrimage from chaos to order, from despair to hope, from darkness to light, and from the prison of self to the liberty of self-mastery.

DIFFICULT TWO-LETTER WORD

Saying “no” is sometimes quite difficult (7). In the past, pharmaceutical companies sponsored many educational activities for physicians with visiting speakers of prominence often providing the presentations. Many physicians responding to a pharmaceutical representative’s request to attend the meeting might answer “yes” or “I’ll do my best to be there.” The latter, I have learned, is simply a rather “gracious” way of saying no. Many of those meetings I have attended through the years have half-empty rooms, and who is paying for those empty chairs? The patients! If physicians and others had simply declined the invitation, there would not have been empty chairs at the meeting. Just like the three-letter word “net” may be the most important word in business, the two-letter word “no” may be the most important word to keep one’s life in good balance. Some people have to practice saying the word. When a request takes one by surprise, a version of “I’ll think about it” might be a ready answer. Delaying an answer, however, usually means an unstated no.

HISTORY OF EXERCISE

According to Amanda Foreman (8), the ancients knew well that people would use any excuse to avoid exercise, bad weather being among the most popular. To counteract the natural human tendency toward inertia (only 1 in 6 American adults does anything like the recommended amount of physical activity), the Greeks had their Olympics, the Chinese their tai chi, and the Indians their yoga. The Romans made exercise a legal requirement for all male citizens aged 17 to 60 years. With some exceptions, like Thomas Aquinas, who was colossally fat, lack of exercise was rarely a problem in the Middle Ages. Few people had time for aerobics when survival was the common thought. The early American settlers were too busy chopping wood and dodging arrows to worry about their overall fitness. By the federal era, things had changed. Thomas Jefferson was appalled by the sedentary habits of his countrymen. “If the body be feeble, the mind will not be strong,” he warned, adding: “Not less than two hours a day should be devoted to exercise and the weather should be little regarded.” His words, however, did little to stop the trend toward indolence. A century later, when the US entered World War I in 1917, military authorities were shocked to discover that one of three draftees was unfit for combat. Washington, DC, responded with a raft of new laws, mandating that physical education be part of every school curriculum. Nevertheless, in the early 1950s, almost 60% of US children failed at least one component, compared with only 9% of children in European countries.

Many poets and prose writers advocated walking. Wordsworth, Coleridge, and Shelley were all noted walkers. The 19th century essayist Thomas De Quincey believed that Wordsworth’s daily walk was responsible for “much of what is excellent in his writings.” Similarly, a 2-mile stroll is said to have inspired John Keats to write his greatest poem, “Ode to Autumn.” Charles Dickens was another great walker, routinely covering 20 miles in a day. During his last trip to the US, he devised a 13-mile walking race for his friends George Dolby and James Osgood. On that February 29, 1868, race day, heavy snow fell. Icicles formed on the men’s beards. Both Osgood and Dolby braved the storm, urged on by Dickens from the comfort of his carriage. He rewarded them afterwards with a “very splendid dinner” with guests including Oliver Wendell Holmes and Henry Wadsworth Longfellow. Dickens repeated often: “Walk and be happy, walk and be healthy. The best way to lengthen out our days is to walk steadily and with a purpose.”

YEARS REMAINING

The Centers for Disease Control and Prevention website provides tables that estimate what happens to Americans from birth to death (9). Starting with 100,000 births, the tables estimate the total number of person-years of life for the group (a person-year is 1 year of life by one person), the number of deaths each year, and the number of person-years remaining at the end of each year. The table stops at age 100. Therefore, the maximum possible number would be 10 million person-years (100 years times 100,000 lives). Even the starting number tells something: instead of 10 million, it is 7,851,473 person-years, a gigantic improvement from the 5,358,122 person-years of 1910. We have gained
CREMATION ON THE RISE

The percentage of US deaths in which remains were cremated in 1960 was 3.6% and in 2012 it was 43.2% (10). That rate is projected to reach 49% by 2017 and 57% by 2025. The tradition of families staying in one town or one state and then being buried in the same place is becoming increasingly less common. Mississippi has the lowest cremation rate at 17%, followed by Alabama, 20%; Kentucky, 22%; Louisiana, 23%; and West Virginia, 26%. The five states with the highest cremation rates are Nevada, 74%; Washington, 73%; Oregon, 71%; Hawaii, 70%; and Maine, 69%. Texas has a cremation rate of 37%. Funeral directors say that many social and religious drawbacks that once kept cremation in check no longer hold sway. The Catholic Church, which once frowned upon cremation, now seems all but resigned to the massive shift in the public’s attitude toward cremation. Although the Catholic Church doesn’t favor cremation, because it believes in the resurrection of the body after death and therefore prefers burial, it does not prohibit the growing practice. The Cremation Association of North America cites five primary reasons why people say they prefer cremation: it saves money (30%), it saves land (13%), it is simpler (8%), the body is not in the earth (6%), and it is a personal preference (6%). Money is clearly the biggest motivation. An average adult funeral cost about $710 in 1960; in 2012, not taking inflation into account, the average funeral was just over $7000. Adding the typically required vault raises the price to nearly $8500. Cremations are less than half the cost of a funeral.

SHAM SURGERY

In a landmark study of a new cardiovascular device unveiled in January 2014, patients received anesthetics, had a large-bore catheter inserted into one of their major arteries, and had contrast material injected into their bloodstream (11). The physicians worked on them for about an hour, with unnecessary pokes and prods, while a monitor displayed the false progress. The patients were not being treated. They had agreed to undergo the angiographic procedure without knowing if they got the real treatment. They were part of the Food and Drug Administration (FDA)—approved study of a new medical device from Medtronic to treat refractory high blood pressure that is resistant to conventional medicines. Some patients were randomly assigned to this sham procedure (placebo group). Was their sacrifice worth it? That question many may want to consider as the FDA insists on a new study methodology with uncertain benefits. The methodology’s high cost means that some new products may be delayed for many years. The goal is to isolate the observed effect of a new treatment from other factors that could affect the results. The blood pressure device works by destroying small nerves in arteries that supply the kidneys. The activity of these nerves contributes to hypertension. The FDA wants to learn if the psychological influence of the procedure, rather than the new device, may lower the blood pressure.

Preliminary results from the sham study suggest that the device might not deliver the hoped-for benefits. While some people think the problem was not with the device but more with the way the procedure was designed in that trial, the negative results are already emboldening proponents of sham studies.

Yet, research that introduces harm or risk with no opportunity for benefit would seem to conflict with the principle governing research on humans. Some of these principles are reflected in the Declaration of Helsinki, an international treaty concerned with the conduct of medical research. Other experiments using sham surgery are obligating patients to undergo unnecessary anesthetics, radiation, abdominal incisions, endoscopy, and injections into the rectum, to mention a few examples. The FDA tries to address ethical issues by letting patients who get sham treatments eventually join the real treatment group, but this often requires a second operation. The sham trials also can be costly because they involve unnecessary procedures. They are hard to recruit for when patients know they may get a false unnecessary operation. All of this raises development costs and encourages firms to skip the US market and commercialize new products overseas. This obviously can suppress innovation. Instead of clinging to inflexible testing requirements, Scott Gottlieb suggests that the FDA should allow trials that are feasible, reflect clinical practice, and are morally defensible. There are methods for evaluating science that do not require such contrived experiments on people.

ATTENTION DEFICIT HYPERACTIVITY DISORDER

The Centers for Disease Control and Prevention released data in March 2013 showing that 11% of school-aged children in the US—6.4 million kids—had received the medical diagnosis of attention deficit hyperactivity disorder (ADHD), a 41% increase in the past decade (12). Over two-thirds of kids with an ADHD diagnosis received prescriptions for stimulants like amphetamine (Adderall) or methylphenidate (Ritalin). The data sparked a debate about whether American children were being overdosed and overmedicated for ADHD.

The diagnosis and treatment of ADHD are spreading globally. In 2010, in Israel, methylphenidate use increased by 76%. The following year a study by Israel’s Health Care Services found that as many as 1 in 5 Israeli children were prescribed stimulants without a proper ADHD diagnosis. Growing awareness of ADHD combined with increasing pressure on children to achieve academically in countries like China, India, South Korea, and Saudi Arabia has led to surging numbers of diagnoses and prescriptions worldwide. Between 2000 and 2010, global ADHD medication sales soared 26% a year to more than $8 billion. The total is projected to reach as high as $14 billion in the next 2 years.

Substantial evidence now shows that ADHD medication, when truly warranted, not only boosts attention but also improves academic performance and a child’s quality of life. But even as global sales surge, evidence accumulates that stimulants...
are no silver bullets. Hundreds of controlled clinical trials have found that while ADHD medications have clear benefits in the short term (measured in months or a few years), the long-term effects are not clear. Prolonged use may in some cases promote brain growth but in other cases alter brain chemistry, eliminating some of the medications’ initial effectiveness.

The pressure to treat ADHD is growing particularly fast in China and South Korea, which are making a strong push to improve academic performance. Many elementary and secondary schools in China force children to sit for hours, attending lectures and cramming for tests. It is only natural that children in these circumstances need help to remain focused. There are signs of some resistance to this trend in Europe. Their health officials advise physicians to resort to medication only after trying behavioral therapy.

MULTIPLE SCLEROSIS AND STATINS

Chataway and colleagues (13) in London studied 70 patients with multiple sclerosis (MS) who took a statin (simvastatin) and found that brain shrinkage, which usually averages 0.6% annually in MS patients, fell to about 0.3% annually, and neurologic function improved after 2 years on 80 mg of simvastatin. The trial suggests another possible benefit of the statin class of drugs.

A RAISE FOR CUBAN PHYSICIANS

Beginning June 1, 2014, hundreds of thousands of medical workers in Cuba will get raises, in some cases exceeding 100% (14). Physicians with two specialties will see their salary go from the equivalent of $26 a month to $67, while a new nurse will make $25 a month. The Communist Party keeps the salaries very low.

DISCOVERIES, INVENTIONS, AND ENVIRONMENTAL CHANGE

In 1858, Edwin Drake began his effort to extract oil from the ground, at a time when all of America relied on whale oil to light its lamps and to lubricate the new machines of the industrial world (15). The USA dominated the whaling industry, which sent its ships on multiyear 10,000-mile journeys from its Massachusetts base of operations around the tip of South America and into the Pacific in pursuit of humpbacks and sperm whales. The blubber from the butchered beasts, melted down into oil, earned New Bedford, Massachusetts, the title of “The City that Lit the World.” The whaling villages of Honolulu and Lahaina in the Hawaiian Islands welcomed 100 to 800 ships a year, until a century of unceasing slaughter depleted the whale populations.

At the same time, tinkerers and entrepreneurs in Pennsylvania began developing petroleum-based lamp oil as a cheaper alternative to the increasingly limited supplies from whaling. In 1851, Samuel Kier began collecting crude oil from puddles and springs near his salt mines. He refined it into the newly patented “kerosene,” inventing a lamp to accommodate his product, promising better and cheaper illumination than whale oil.

But it remained for Drake, a former railroad conductor, to devise a way to get more of the petroleum from below the earth’s surface. His well near Titusville, mocked as “Drake’s Folly,” took almost a month to reach a depth of 70 feet. It employed Drake’s revolutionary concept of using piping in the bore hole so rocks surrounding the drill shaft wouldn’t collapse and close the bore hole. He never patented the process and died in poverty 22 years later. But his engineering genius saved the whales!

Oil drilling facilitated the mass production of kerosene, which quickly replaced whale oil as the fuel of choice for lighting. The mighty whaling industry, which employed an estimated 70,000 persons at its peak, dwindled to near extinction, saving the shrinking whale populations from near-certain extinction. The emerging oil industry eventually added 100 times the jobs of the whaling business it replaced. Meanwhile, automobiles fed by the extracted oil made their own huge contribution to environmental enhancement. Though reviled today as sources of air pollution and global warming, cars initially replaced the millions of horses whose prodigious droppings and rotting carcasses fouled every major 19th century city with a potent and indelible stench.

In the same way, according to Michael Medved, a raft of yet unforeseen breakthroughs, providing the promise of profit for their intrepid developers, will do more to address our environmental challenges than even the most sweeping legislation or the most anguished pleas for conservation.

EMPLOYED VS. UNEMPLOYED

We all know about the unemployment rate, but there is relatively little discussion about the employment rate or the employment-to-population ratio, which measures the share of all potential workers who have a job (16, 17). This measure in 2007 was 62% on average, 60% in 2009, and 59% in 2013. The jobless rate has fallen to nearly 6% from 10% in October 2009, and the private economy for the first time has regained all the jobs lost to the financial panic. But the unemployment rate underestimates the jobs problem, because people who stop looking for a job no longer count as “unemployed” in the official tables. In a normal economy, the employment and unemployment rates have an inverse relation: when one rises the other falls and vice versa. But in the current economy, the unemployment rate is falling but the employment rate has fallen too. Former workers are simply leaving the economy or sitting on the sidelines. The labor force participation rate, which measures the active portion of available workers not including dropouts, now stands at just over 63%, a level last seen in 1978.

Many attribute the decline of work in America to the wave of baby boomers heading into retirement and the fact that the population at large is getting older. This view is probably amplified by workers who retire earlier because they lost their job and cannot find a comparable one. Yet, the decline in work is also affecting those between the prime working ages of 25 and 54 years. The employment rate for those workers rose steadily in the postwar period, dipping during recessions but always returning to an upward climb. The rate reached an all-time high in 1999 at 82%, dipped in the early 21st century, and was recovering until the recessionary collapse. At just under 77% today, this measure of work has only recently returned to the 2009 levels. That’s roughly where it last hovered in 1984 and 1985 before climbing amid the Reagan growth surge. So, after a 2% annual economic growth since 2009, the share of mid-career workers in their best earning years who are on the job is still historically low. In recent years incentives to not work have also accentuated the problem—it is easier to get
HEROIN RESURGENCE

A conference of >200 officials, organized by the Police Executive Research Forum, met in Washington, DC, in April 2014 to discuss the resurgence of heroin after its former popularity in the 1950s and 1960s (18). A survey by the Police Executive Research Forum of 170 US police agencies cited heroin as their communities’ top drug problem: heroin, 36%; marijuana, 23%; methamphetamine, 20%; prescription pills, 7%; and crack cocaine, 6%. Heroin and other opiates are now claiming more lives in many communities than violent crime and car crashes. Several reasons appear to account for its new popularity: it’s more available and more pure than previously, and it is less expensive than prescription opiates, costing from $4 a bag in some places to $20 in others, making it an attractive drug of choice. In New York City in 2012, there were 730 drug overdose fatalities, with half of those estimated to be related to heroin and prescription opiates, nearly double the number of homicides. The National Drug Threat Assessment rates heroin as the second greatest drug risk, after the abuse of methamphetamine. Attorney General Eric Holder speaking at the conference stressed that the heroin problem was national and urged police and other first responders to carry the drug naloxone, more commonly known as Narcan, that helps resuscitate victims from potentially deadly overdoses.

SYNTHETIC MARIJUANA

Thirty-eight patients came to Dallas’ hospitals in a 2-day period in April 2013 with signs of severe intoxication and psychosis and were suspected of marijuana overdose (19). Some of the patients had to be sedated, and others were restrained and carried into the emergency room by hospital personnel. Some of the patients had increased aggression and tachycardia. Fifteen other patients were treated in a single day in Austin during the same week for suspected synthetic marijuana overdose. A new danger!

INSTITUTIONAL GENERAL MEDICAL AND SURGICAL JOURNALS

Through the years, many institutions at one time or another had their own medical journals, but most with time vanished, most commonly for lack of financial support. One of the oldest and most successful was the Bulletin of the Johns Hopkins Hospital, which began in 1889 (3 years before the hospital opened) and continued under that name until 1949, when the name was changed to The Johns Hopkins Medical Journal which, to my great disappointment, was discontinued in 1966. A number of classic medical articles were published in its pages.

The Proceedings of the Staff Meetings of the Mayo Clinic (Figure 1a) began in 1926 (about 4 decades after the clinic started). Its name was changed to Mayo Clinic Proceedings in 1964, and it continues going strong. It too has published its share of classic articles through the years. The monthly issues are now published by Elsevier.

The Cleveland Clinic Journal of Medicine (Figure 1b) was started in 1931, 10 years after the clinic’s founding, and it has been going strong ever since. Like the Mayo Clinic journal, the Cleveland Clinic Journal of Medicine goes to >100,000 physicians and is widely read.

The Baylor University Medical Center Proceedings (Figure 1c) is a recent addition, having started in 1988 by Dr. George J. Race, 85 years after the hospital was founded. Nevertheless, it now goes to >7000 physicians and is indexed in PubMed and as a consequence it receives 2 million internet “hits” yearly. The number of articles published in the BUMC Proceedings now exceeds the number of articles published in a 3-month period in the Cleveland Clinic Journal of Medicine and is not far behind that of the Mayo Clinic Proceedings.

CERTIFICATION BOARD SCAMS

In May 2014, I received a letter from the American Board of Cardiology Committee on Honors and Awards, dated May 9, 2014, and signed by A. J. Alaa Windsor, MD (Figure 2). I was a bit surprised and transiently honored when I read the letter until I got to the second page, which indicated that there were actually three engraved award plaques: one read The American Board of Cardiology Award of Honor for 2014; another The Distinguished Master Laureate of the American Board of Cardiology; and the third Senior Consultant to the American Board of Cardiology. Under each of these was the option to order a number of plaques. Near the bottom of the second page was the following: “Please assist in the funding of this program of recommendation of excellence. Please enclose registration fee of $300 made to: American Board of Cardiology. Please enclose engraving and preparation fee of $70 for each 10” × 8” engraved plaque and $15 for shipping
and handling of each plaque.” Also at the top of this second page is a declaration related to acceptance of the award:

I hereby accept the American Board of Cardiology Award of Honor and the designation as Master Laureate of the American Board of Cardiology Award. I promise to continue to uphold the centuries old traditions of excellence and humanitarianism in medicine and shall continue to practice medicine in accordance with the Oath of Hippocrates, the Ten Commandments, and the Golden Rule to treat others as I would have others treat me. And I will continue to always faithfully work to support and promote excellence, education, compassion, kindness and truest humanitarianism in medicine.

I thought about this particular document overnight and became leery, and the next day searched for A. J. Alaa Windsor, MD, on Google and could not find one thing on him. My assistant, Becky Banks, found that the American Board of Internal Medicine (ABIM) provided the following scam warning on its website:

ABIM has received reports from several of our diplomates regarding letters and solicitations they have received from groups offering “certification” in Geriatric Medicine, Cardiology and Hospital Medicine, among other things. ABIM is concerned about the welfare of patients who may choose doctors representing themselves as “board certified” based on their possession of a certificate from unaccredited “boards” that award certificates but require no accredited training, testing or medical background review. . . . If you hear from them, or receive any certification information that seems suspicious, ABIM would like to know about it (abim.org/news/scam-certification-boards.aspx).

William Clifford Roberts, MD
12 May 2014

15. Medved M. Innovation will heal the planet. USA Today, February 19, 2014.
18. Johnson K. Heroin a growing threat across USA, police say. USA Today, April 17, 2014.
Dear readers,

We are committed to keeping Baylor University Medical Center Proceedings available in print form, as well as electronically. We believe that print offers advantages over electronic: It’s easier to browse and easier to share with others or place in your waiting rooms. There is a cost for print, however, at a time when budgets are being cut. Thus, we are asking for donations—and will do so yearly. Please consider making a donation online at https://give.baylorhealth.com/how-to-donate/donate-online (just choose BUMC Proceedings from the drop-down menu).

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We also want to stress that while “Baylor University Medical Center” is in the journal’s title, the journal belongs to the entire Baylor Scott & White Health system. We’ve added the new system logo on the back cover and featured images from various hospitals in the system. We also gladly accept submissions from throughout Baylor Scott & White Health, and outside the system as well. Our goal is to publish the best submissions.

With kind regards,

William C. Roberts, MD
Editor in chief

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