To access Baylor’s physicians, clinical services, or educational programs, contact the Baylor Physician ConsultLine: 1-800-9BAYLOR (1-800-922-9567)

Baylor University Medical Center Proceedings
The peer-reviewed journal of Baylor Health Care System, Dallas, Texas

Multipatient Studies

363 Migraine disability, healthcare utilization, and expenditures following treatment in a tertiary headache center
F. G. Freitag, H. Lyss, and G. R. Nison

368 Advance care planning knowledge and documentation in a hospitalized cancer population
A. Barakat, S. A. Barmen, M. A. Casanova, M. J. Stone, K. M. Shuey, and A. M. Miller

373 Incidence and severity of respiratory insufficiency detected by transcutaneous carbon dioxide monitoring after cardiac surgery and intensive care unit discharge
E. E. Lapow, B. Loper, L. W. Jennings, and M. A. E. Ramsay

376 Outcome assessment of 603 cases of concomitant inferior turbinectomy and Le Fort I osteotomy

Single-Patient Studies

382 Copper deficiency (hypocupremia) and pancytopenia late after gastric bypass surgery
S. D. Robinson, B. Cooper, and T. V. Leday

387 Isolated atrial amyloidosis and the importance of molecular classification

390 The Heerfordt-Waldenström syndrome as an initial presentation of sarcoidosis
M. C. Denny and A. D. Fotino

393 Unusual dermal pleomorphic calcifications in a case of inflammatory breast carcinoma

396 Basal cell adenoma of the breast
M. Van Vrancken, M. Mir, and W. Herlihy

398 Critical lower limb ischemia from an embolized Angio-Seal closure device
C. Dintiri, R. E. Konaw, G. Feighan, S. Rottey, R. C. Sklar, and J. W. Dri

401 The myth of the Bernheim syndrome
M. S. Chung, J. M. Ko, T. Chamogeorgakis, S. A. Hall, and W. C. Roberts

405 Fibromuscular dysplasia of the renal artery as a cause of secondary hypertension
A. Y. Hundae, C. A. Hebert, and J. M. Schussler

407 Slow group beating
D. L. Glancy and V. A. Lathia

408 Continuous murmur and cardiac failure in a 53-year-old woman
D. L. Glancy and E. B. Hanna

410 Angiotensin overuse
T. Patel, D. Tietze, and A. N. Mehta

Historical Studies

417 Consults for conflict: the history of ethics consultation
Elliot B. Tapper

Editorials

423 What’s going on in dental education?
Eric S. Solomon

425 An unforgettable, perpetual medical student, 1961
S. Robert Lathan

Book Reviews

427 Review of For the Love of Wild Things (Dimijian)
Daniel E. Potter

428 Review of Sifting Shades (Khan)
Harbans Lal

From the Editor

432 Facts and ideas from anywhere
William C. Roberts

Miscellany

386 Aversions: Photograph by Dr. Rosenthal
412 Baylor news

416 Clinical research studies enrolling patients
429 Reader comments: Cardiac rehabilitation in firefighters

442 Selected published abstracts of Baylor researchers

447 Instructions for authors
Dallas 2013

Register for Scientific Sessions, in your backyard this November 16–20 — the leading cardiovascular meeting in the United States with more than 18,000 cardiovascular experts from over 105 countries, in addition to more than 1.5 million virtual professional attendees.

Basic Science  Clinical Science  Translational Science  Population Science

Lead the way to discovery in the fight against cardiovascular disease and stroke. Register today!

Exhibits  Nov. 17–19
Scientific Sessions 2013  Nov. 16–20
Resuscitation Science Symposium  Nov. 16–17
Cardiovascular Nursing Symposium  Nov. 19–20
PVD FIT Workshop  Nov. 16

Don’t Miss at Scientific Sessions 2013:
• More than 5,000 presentations from:
  − 1,000 invited faculty
  − 1,000+ abstract presenters (oral and poster)
• Late-Breaking Clinical Trials
• Late-Breaking Basic Science
• Best of AHA Specialty Conferences
• Global Congress on Physical Activity — Featuring leading experts on physical activity and fitness from around the world in the areas of epidemiology, basic and clinical science, prevention science, rehabilitation, public health and governmental policy.
• Case Theaters: Learning at the Movies
• Early Career/PVD Fellows in Training Workshop
• International Joint Sessions
• 26 Programming Tracks — Tracks cover basic, translational, clinical and population science to focus your education on your specialty or expand your knowledge in other areas.
Migraine disability, healthcare utilization, and expenditures following treatment in a tertiary headache center

Frederick G. Freitag, DO, Heidi Lyss, MBA, and George R. Nissan, DO

Headache is among the most common disabling pain complaints. While many patients are managed in primary care or referral neurology practices, some patients have refractive situations that necessitate referral to a tertiary headache center. Increasing frequency of headache is strongly associated with increasing disability and workplace absenteeism as well as increased healthcare utilization. Previous studies have demonstrated that headache care in a dedicated tertiary center is associated with a decrease in headache frequency and improvement in other characteristics that persist over extended periods of time. Previous studies have not examined the impact of this treatment on subsequent healthcare utilization and associated expenditures. In this study we examined the changes in healthcare utilization and expenditures as well as the impact on disability and workplace productivity with treatment in a tertiary headache care center that used initial treatment settings of inpatient and outpatient care and considered the difference between those with episodic migraine and those with chronic migraine and its complications. Tertiary care was found to produce positive reductions in disability, healthcare utilization, and expenditures. These results suggest that earlier tertiary-level intervention may avoid the complications of migraine that occur in some patients and the increasing costs and utilization of care associated with higher disability.

Inpatient dedicated programs for headache were developed to care for patients with difficult-to-resolve headaches. Patients treated in dedicated headache treatment centers have been shown to realize more robust outcomes. These programs seek to provide comprehensive assessment and treatment for patients and address the lifestyle, behavior, and physical factors that contribute to disease management. A variety of outcomes may be considered for headache management, including pain severity, headache frequency, amount of medication taken, quality of life, disability, productivity, healthcare costs, and absenteeism and “presenteeism,” which describes patients’ limited functioning from headache at work. Existing outcome studies of headache treatment have focused almost exclusively on measures of headache attributes, with results reported in the US Headache Consortium Inpatient Treatment guidelines (1). These studies have noted significant reduction in the frequency and severity of headaches over both short-term and long-term assessments when headaches were treated in an integrated inpatient program. Disability or healthcare costs have largely gone unstudied (1), and few studies have evaluated the outcomes of treatment for patients in tertiary headache centers in which hospitalization has not been a component of the treatment program. Some research has evaluated the effects of migraine on quality of life. The Migraine Disability Assessment Score (MIDAS®) was developed in 1997 to assess the impact of periodic migraine on lost time and productivity at work, at home, and in family activities (2–4) in patients with episodic headache. Episodic headache has been defined as headache that occurs on 14 or fewer days per month, whereas chronic headache has been defined as occurring on 15 or more days a month for at least 3 months (5). The MIDAS was not developed for use in patients with daily or nearly daily headache. Mathew and colleagues (6) examined the MIDAS tool in patients with very frequent headaches in a tertiary setting and found that even among these patients, treatment outcomes could be assessed with the MIDAS. In an earlier study (7), we found a correlation between higher MIDAS scores and greater healthcare expenditures and utilization and found that greater reductions in MIDAS scores correlated with greater reductions in healthcare utilization. In recent years, increasing interest has focused on utilization of healthcare resources and corresponding costs of care (8–10). Given both the findings and limits of studies to date that look at the various impacts of migraine, the current research was conducted to assess the following variables before and after treatment in a specialized tertiary headache treatment center: 1) changes in episodic and chronic migraine headache attributes; 2) changes in quality of life as measured by patient MIDAS scores; 3) changes in healthcare utilization and costs; and 4) changes in patient absenteeism and presenteeism at work and in family and community functions.

METHODS

Participants were treated at a tertiary headache center at a large teaching hospital. The inpatient program as well as the

From the Comprehensive Headache Center, Baylor Neuroscience Center, Baylor University Medical Center at Dallas (Freitag, Nissan); and Heidi Lyss Consulting, Moraga, California (Lyss). Dr. Freitag is now with the Medical College of Wisconsin.

Corresponding author: Frederick G. Freitag, DO, Department of Neurology, Medical College of Wisconsin, 9200 West Wisconsin Avenue, Milwaukee, WI 53226 (e-mail: dhcdoc@gmail.com).

Proc (Baylor Univ Med Cent) 2013;26(4):363–367
connected outpatient program provide comprehensive multidisciplinary assessment and treatment. The patient’s diagnosis was determined by the treating physician, without necessarily aligning with the International Classification of Headache, while treatment setting and specific treatments were determined by the clinician with the patient. Diagnoses included in this study were episodic migraine and chronic migraine, with and without medication overuse. Specific medical therapies were not evaluated separately.

Patients selected for outpatient treatment were provided with acute and preventive medications for their headaches. They were instructed in lifestyle modification and were offered a variety of nonpharmacologic strategies as part of comprehensive treatment. Not all patients treated on an outpatient basis were provided with a full array of nonpharmacologic strategies due to limited access to care for some of these services. Patients treated as inpatients not only received acute and preventive medications, but also were discontinued from other acute medications that had been causing medication overuse headache. This discontinuation has been demonstrated to play a significant role in treatment outcome (11–13). Inpatients were treated with intravenous dihydroergotamine and given additional adjunctive intravenous medications based on their clinical situation in order to break their headache cycle. In addition to receiving the educational component as did the outpatient group, inpatients were evaluated by psychological services, underwent counseling, and received behavioral interventions including biofeedback, physical therapy, and dietary education. Many of these services were provided during their hospitalization, and some were continued following the patient’s discharge to the outpatient setting.

All new patients to the center were invited to participate in the study. These patients came to the tertiary headache center from a range of geographic locales around the United States. Those who expressed interest in participating provided written informed consent using a form approved by the hospital institutional review board. Five hundred consecutive new patients to the clinic were included in this evaluation process. Enrollment occurred on a continuing basis over a period of approximately 6 months. Of the 500 patients approached to participate in this study, 371 completed the first phase of the data collection and 294 completed the follow-up phase of the data collection (Figure 1).

The first phase of data collection consisted of a series of self-reported questionnaires regarding headache traits, prior treatments, use of healthcare resources related to headaches and general health, and associated expenses incurred, including both out-of-pocket and insurance-reimbursed expenses. In addition, participants were required to complete a MIDAS survey for the prior 3 months before their first visit, and their resulting score was used to assess their headache frequency. The data from the healthcare utilization questionnaires examined the 6 months prior to their first visit to the tertiary headache center. In addition they were informed that they would be asked to complete a similar assessment following their initial assessment and treatment at the center. The second phase was conducted at least 3 months and less than 6 months after completion of the patient’s first treatment program at the clinic and/or in the inpatient treatment unit. The final collection of data occurred approximately 1 year after the first patient was enrolled.

Patient data were blinded to the physician reviewer through a numeric code assigned to each patient. An administrator of the center maintained the log of the patients, their contact information, and their assigned numeric codes. All data were entered into an Excel spreadsheet by the center administrator and provided to the physician reviewer.

RESULTS

The total population that provided complete data consisted of 294 patients; 94 of these patients had episodic migraine diagnoses, 153 had chronic migraine diagnoses, and 47 had other headache diagnoses, such as tension-type headache, cluster headache, and posttraumatic headache, representing a heterogeneous group that provided too few patients with any one diagnosis to provide meaningful assessment. Their data, while included in the data set comparing inpatient versus outpatient treatment groups (Table 1), were not further examined as a separate group in this study.

Patients’ initial data demonstrated that they had headaches on more days than not and had MIDAS scores far in excess of the MIDAS score range used to describe patients as significantly disabled. Patients were seen by their prior treating physician an average of once per month. Emergency department utilization averaged at least one visit every 6 months, and an inpatient treatment in the patient’s home locale had occurred an average of once every 2 years. Estimated healthcare expenditures averaged more than $10,000 per year. Following treatment at the tertiary level, significant reduction in

![Figure 1. Subject enrollment outcomes.](image-url)
healthcare utilization occurred broadly and robustly in both the inpatient group and outpatient group, aside from the finding that inpatient readmission occurred more frequently in those who were initially treated at the tertiary care center as inpatients (Table 1).

The migraine population of patients in the study represented a group with more significant frequency of migraines—an average of 17 days per month—compared to the US population, with its average of 2 headache days per month. Even the episodic migraine group treated at the tertiary headache center on an outpatient basis averaged 23.2 headache days for the 3 months prior to their first visit to the center, roughly half the average number of headache days experienced by a typical new patient to the center who was admitted for inpatient treatment of episodic migraine. The episodic migraine group overall was somewhat younger on average and less prone to comorbid diseases, with a shorter headache history of 12.5 years compared with 15.3 years for the chronic migraine population. During the 90 days prior to initial treatment at the tertiary center, the outpatient episodic migraine group not only experienced 50% fewer headache days than the inpatient migraine group, but also had approximately 50% lower MIDAS scores, one third the emergency department visits, and one fifth the prior hospital admissions compared with the group treated by the center as inpatients. Following initial treatment, the inpatient migraine group realized more robust reductions in healthcare costs (–47%), physician visits (–73%), emergency department visits (–80%), and subsequent inpatient care (–88%) than the outpatient treatment group (–22%, –6%, –12%, and +510%, respectively). The mean length of initial hospitalization was 7.4 days, and its costs were included in the posttreatment assessment. Subsequent hospital admissions increased substantially in the outpatient group (Table 2).

About half of the patients with chronic migraine were diagnosed with concomitant medication overuse (Table 3), whether they initiated treatment in the outpatient or inpatient setting at the tertiary headache center. Those with chronic migraine without medication overuse were treated at the center as outpatients approximately half as often as they were treated as inpatients. By contrast, those with medication overuse headache with chronic migraine were twice as likely to be treated as outpatients since many migraines with medication overuse are not toxic and outpatient bridge treatments can be effective for transition of this condition. All four groups were close in mean age and frequency of comorbid medical illnesses. Chronic migraine patients with medication overuse tended to have a longer history of disease than chronic migraine patients without medication overuse. Headache days per 3 months prior to the initial visit and MIDAS scores were highest in the population with medication overuse, regardless of treatment setting. These same patients had the greatest reduction in these same parameters over the evaluation period. Physician and emergency department visits declined by roughly the same level of magnitude in all treatment groups. Hospital admissions decreased by roughly 50% in those with chronic migraine without medication overuse headache who were treated as outpatients and in those with medication overuse who were treated as inpatients. Conversely, a significant increase in readmissions occurred in the other two chronic migraine groups.

Healthcare costs changed to only a limited degree in patients with chronic migraine, with the exception of those chronic migraine patients with medication overuse who were treated in a multidisciplinary inpatient unit. For this group, post-inpatient treatment costs declined by one third from pretreatment costs. Overall, healthcare costs were 2 to 3 times higher in patients with medication overuse as compared to the non–medication overuse chronic migraine population.

**DISCUSSION**

The burden of migraine and chronic migraine has been demonstrated in the American Migraine Prevalence and Prevention Study. Despite this result, these disorders receive little in the way

### Table 1. Patient characteristics and outcome data for migraine treatment for all patients, treated in both inpatient and outpatient settings

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All inpatient initial treatment</th>
<th>All outpatient initial treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>116</td>
<td>178</td>
</tr>
<tr>
<td>Age (mean in years)</td>
<td>48.9</td>
<td>49.3</td>
</tr>
<tr>
<td>Number of comorbid medical illnesses</td>
<td>2.54</td>
<td>1.48</td>
</tr>
<tr>
<td>Headache disease duration (years)</td>
<td>14.2</td>
<td>14.6</td>
</tr>
<tr>
<td>Cost/6-month period</td>
<td>Pretreatment $6698 Posttreatment $4384 Change $2314</td>
<td>Pretreatment $5484 Posttreatment $4290 Change $1194</td>
</tr>
<tr>
<td>Number of headache days/3 months</td>
<td>56.6</td>
<td>42.4</td>
</tr>
<tr>
<td>MIDAS</td>
<td>83.4</td>
<td>27.1</td>
</tr>
<tr>
<td>Number of MD visits for headache/6 months</td>
<td>6.58</td>
<td>1.36</td>
</tr>
<tr>
<td>Number of ED visits for headache/6 months</td>
<td>1.65</td>
<td>.53</td>
</tr>
<tr>
<td>Number of inpatient admissions/6 months</td>
<td>0.29</td>
<td>.37</td>
</tr>
</tbody>
</table>

MIDAS indicates Migraine Disability Assessment Score; MD, physician; ED, emergency department.
of specific acute and appropriate levels of preventive care (14). The significance of this absent or insufficient care, even in the episodic migraine population, has been underrecognized. The direct costs for migraine are expected to exceed $11 billion annually and be over $2500 per person with migraine compared to matched controls (14). The Affordable Care Act will require delivery of quality care in a cost-effective manner. One issue that is rarely considered in this process is the burden on the employer and employee in lost time and productivity related to the disorder. Migraines cost employers $2444 per year per patient for women in their peak productive years who have episodic migraine, and over $7100 per year for those with chronic migraine. In men, this increases to over $4100 per year per patient with episodic migraine and almost $13,000 per year for chronic migraine (15). As with many disorders, the greatest costs of treatment will be for a small percentage of patients who have frequent headache and poor response despite being provided with the best-evidence treatments. In the present study, we have demonstrated that there are patients who have realized substantial benefits from treatment in the tertiary setting. These improvements have been realized in parameters of headache frequency, disability, healthcare utilization, and the costs of that care.

Table 2. Patient characteristics and outcome data for patients with episodic migraine, treated in both inpatient and outpatient settings

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Inpatient initial treatment</th>
<th>Outpatient initial treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>25</td>
<td>69</td>
</tr>
<tr>
<td>Age (mean in years)</td>
<td>46</td>
<td>47</td>
</tr>
<tr>
<td>Number of comorbid medical illnesses</td>
<td>2.2</td>
<td>2.1</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>9.9</td>
<td>13.5</td>
</tr>
<tr>
<td>Pretreatment Cost/6 months</td>
<td>$4787</td>
<td>$2468</td>
</tr>
<tr>
<td>Pretreatment Number of headache days/3 months</td>
<td>47.2</td>
<td>23</td>
</tr>
<tr>
<td>Pretreatment MIDAS</td>
<td>82.1</td>
<td>43.2</td>
</tr>
<tr>
<td>Pretreatment Number of MD visits/6 months</td>
<td>8.8</td>
<td>2.4</td>
</tr>
<tr>
<td>Pretreatment Number of ED visits/6 months</td>
<td>1.68</td>
<td>.33</td>
</tr>
<tr>
<td>Pretreatment Number of inpatient admissions/6 months</td>
<td>.48</td>
<td>.06</td>
</tr>
</tbody>
</table>

MIDAS indicates Migraine Disability Assessment Score; MD, physician; ED, emergency department.

Table 3. Patient characteristics and outcome data for patients with chronic migraine, with or without medication overuse headache, treated in both inpatient and outpatient settings

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Chronic migraine without medication overuse</th>
<th>Chronic migraine with medication overuse</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Outpatient treatment</td>
<td>Inpatient treatment</td>
</tr>
<tr>
<td>Number of patients</td>
<td>27</td>
<td>46</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48</td>
<td>50</td>
</tr>
<tr>
<td>Comorbid medical disorders</td>
<td>2.8</td>
<td>2.8</td>
</tr>
<tr>
<td>Disease duration</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>Pretreatment Cost/6 months</td>
<td>2724</td>
<td>2646</td>
</tr>
<tr>
<td>% Change</td>
<td>−2.8%</td>
<td>−11.5%</td>
</tr>
<tr>
<td>Pretreatment Headache days/3 months</td>
<td>54.4</td>
<td>48.1</td>
</tr>
<tr>
<td>% Change</td>
<td>−49.9%</td>
<td>−11.5%</td>
</tr>
<tr>
<td>Pretreatment MIDAS</td>
<td>55.1</td>
<td>59.2</td>
</tr>
<tr>
<td>% Change</td>
<td>−39.9%</td>
<td>−9.9%</td>
</tr>
<tr>
<td>Pretreatment MD visits/6 months</td>
<td>5.18</td>
<td>6.8</td>
</tr>
<tr>
<td>% Change</td>
<td>−89.2%</td>
<td>−81%</td>
</tr>
<tr>
<td>Pretreatment ED visits/6 months</td>
<td>1.27</td>
<td>1.41</td>
</tr>
<tr>
<td>% Change</td>
<td>−70.3%</td>
<td>−55.3%</td>
</tr>
<tr>
<td>Pretreatment Inpatient admissions/6 months</td>
<td>.42</td>
<td>.18</td>
</tr>
<tr>
<td>% Change</td>
<td>−57.1%</td>
<td>+211%</td>
</tr>
</tbody>
</table>

MIDAS indicates Migraine Disability Assessment Score; MD, physician; ED, emergency department.
This study suffers from issues that create some challenges in evaluation, including patients lost to follow-up and verifiable accuracy of financial reporting data. Second, the diagnoses assigned to the patients were clinically applied and hence did not necessarily meet the International Headache Classification criteria. Another issue relates to the nature of the comorbidities and the failure to secure behavioral or psychiatric diagnoses as part of these comorbidities. A study by Lafata and colleagues suggested that the diagnosis of depression as comorbidity to headache may be a driver of the costs of healthcare delivery in these patients (16). In addition, specific data regarding neuroradiological services were not collected. Lastly, while we have obtained an appreciation of the disease duration of headache and some of the issues that might impact response to treatment, we did not collect detailed data to assess for the extent and quality of care of patients prior to initiation of tertiary headache care.

Comprehensive programs for episodic migraine appear from our findings to be effective in positively impacting multiple headache parameters for patients. These patients as a whole, regardless of treatment setting, experienced significant reduction in healthcare utilization. A decrease in MIDAS score results in a substantial reduction in disability parameters. Regardless of the diagnosis or how refractive the patient’s headache has been to previous treatments, it is likely that patients would benefit from tertiary care and realize decreased disability, fewer headache days, and lower healthcare utilization after treatment.

Patients initially treated as inpatients, while improving across the various parameters in similar levels of magnitude compared to the outpatient group, never “caught up” with the outpatient group over the time frame of evaluation. Rather, they had improvements that led them to resemble the baseline for the outpatient group.

The chronic migraine groups were on average older, with more comorbid medical disorders and a longer average duration of disease than that found in the episodic migraine groups. Those with medication overuse were again older and with longer disease duration than those without medication overuse. Patients with chronic migraine without medication overuse were more closely aligned with the episodic migraine groups, though again they had a tendency to have higher service utilization, MIDAS scores, and costs of care than the episodic group. With treatment, however, this group tended to resemble a composite of the episodic migraine groups. Those patients with chronic migraine with medication overuse and those with chronic migraine without medication overuse who were treated initially as inpatients tended to have headache days, MIDAS scores, healthcare utilization, and costs of healthcare higher than any of the other groups and to realize smaller declines in healthcare costs with tertiary treatment.

Factors such as patient compliance with the program over the extended course were not evaluated as part of this study, but have been shown to be a critical factor in the potential to reverse the course of a chronic disorder such as high-frequency migraine (17). Ongoing assessment of treatment programs, patient selection, and evaluation of other therapeutic and diagnostic issues may afford greater clarity and guidance to the process of optimizing treatment outcomes in a cost-effective manner.

Advance care planning knowledge and documentation in a hospitalized cancer population

Ayman Barakat, MD, Sunni A. Barnes, PhD, Mark A. Casanova, MD, Marvin J. Stone, MD, Kathleen M. Shuey, MS, RN, and Alan M. Miller, MD, PhD

To have a better understanding of our patients’ knowledge of advance directive planning and execution, as well as communication with their oncologists regarding their wishes, we conducted a survey on our inpatient hematology-oncology services. A total of 68 unique hospitalized patients with a diagnosis of cancer completed surveys. Surveys were given to all oncology patients regardless of their reason for admission. Overall, 29% of the patients reported having had a discussion with their oncologist regarding their wishes if they became seriously ill or near death. Of those who did have this conversation, the majority said that they, rather than their physician, initiated it. Although the vast majority of patients (97%) knew what a living will was, only 54% had one in place. Twenty patients had a discussion with their oncologist, and 14 of them (70%) had a living will. This percentage was higher than in the group that did not have a conversation with their physician (48%; 23 of 48 patients), but the difference was not statistically significant. Most cancer patients admitted to an inpatient oncology unit either did not have or did not recall having a discussion with their oncologist regarding end-of-life issues. This study gives us a baseline of information in evaluating future interventions directed to improve the quality of patient-physician communication regarding end-of-life planning.

The diagnosis of cancer provides challenges to patients, their families, and their medical providers. Initially, the objective for medical oncologists is to find a cure or at least a treatment to reduce symptoms and prolong survival of their patients. Having a discussion about an advance directive (AD) or end-of-life (EOL) issues with patients at this time may seem counter-intuitive to physicians. More importantly, it may be seen by patients as a confirmation of their fear that they are going to die from this disease. Many times this conversation is avoided until the disease progresses or is refractory, or the conversation never occurs.

Ideally individuals should have sufficient time to think about and discuss these issues with health care providers and others long before they have a life-threatening disease. The 2005 Gallup Public Opinion Poll reported that 40% of Americans over age 18 had a living will (1). Various other public opinion polls report figures of 25% to 40%. In a survey of primary care physicians in Northeastern Ohio, 97.5% of physicians reported comfort with discussing advance care planning, yet reported having those discussions with only 43% of appropriate patients (2). Thus, even though health care providers understand the benefit of EOL discussions with their patients, they initiate such discussions less than half the time.

Oncology patients have a relatively high chance of dying from their disease, yet a national survey of physicians caring for cancer patients concluded that most physicians did not discuss EOL options until symptoms were significant and/or there were no further treatment options (3). A recent study by Zhang et al of 603 patients with advanced cancer reported that only 31% of patients had EOL discussions with their physicians (4). In that study, EOL discussions were associated with significantly lower health care costs in the final week of life. The majority of cancer patients surveyed in one German study wanted their physician to initiate a discussion about writing an AD only if their physician thought it appropriate (5). Almost 80% of physicians in that study thought that they should initiate the discussion if appropriate, but only 17% thought it should be a routine matter as compared to 27% of the patients and 46% of healthy controls.

Another study of patients admitted to a hematology-oncology inpatient service in Virginia provided information about their preferences and attitudes toward AD and which physicians they preferred to host the discussion (6). Of the 75 patients enrolled in the study, nearly all (95%) thought that discussing an AD was very or somewhat important, but only 41% had an existing AD. When asked which physician they would prefer to discuss AD with if it were necessary, 48% indicated their oncologist—but only 7% of the patients actually had this discussion with their oncologist. In a report by Mack et al in a study of over 2000 patients with stage IV lung or colorectal cancer, 73% had EOL discussions identified by at least one source; however, oncologists documented EOL discussion with only 27% of their patients (7).

We conducted a survey on the hematology-oncology inpatient service at Baylor University Medical Center at Dallas from the Baylor Charles A. Sammons Cancer Center (Stone, Shuey, Miller), the Department of Quantitative Sciences (Barnes), and the Department of Internal Medicine (Casanova), Baylor University Medical Center at Dallas. Dr. Barakat is now at the Tulsa Cancer Institute, Tulsa, Oklahoma.

Corresponding author: Alan M. Miller, MD, PhD, Baylor Sammons Cancer Center, Baylor University Medical Center at Dallas, 3410 Worth Street, Dallas, TX 75246 (e-mail: alan.miller@BaylorHealth.edu).
regarding AD and patient-physician communication. The purpose of the survey was to establish baseline information to use to evaluate the effectiveness of future interventions regarding AD and EOL planning.

METHODS

From September 2011 to May 2012, inpatients in the oncology and blood and marrow transplantation units at Baylor University Medical Center at Dallas were surveyed to determine the frequency and effectiveness of EOL discussions between patients and their oncologists. Surveys were given to all oncology patients regardless of the reason of their admission, excluding only those who were unable to speak English and those in any type of medical isolation.

A printed questionnaire with 26 questions was created and distributed (Table 1), along with a cover letter explaining the project. In addition, one of the research nurses verbally explained the project to each patient. After completing the survey, patients placed it in an envelope, sealed it, and returned it to a nurse. Completed surveys were collected on a weekly basis.

Approval for the study was obtained from the Baylor University Medical Center at Dallas institutional review board. The surveys had no patient-identifying information; therefore, the results were anonymous.

Univariate analysis was performed using $\chi^2$ tests, and multivariate analysis was done using logistic regression with Proc Logistic. The SAS statistical analysis system (SAS Institute Inc., Cary, NC) was used for data analysis. Statistical significance was defined as $P < 0.05$ with a two-tailed test. Categorical variables were expressed as percentages and continuous variables as mean ± SD, unless otherwise stated.

RESULTS

Surveys were distributed to 100 oncology patients, and 91 completed surveys were returned. Twenty-three patients submitted more than one survey over different hospital admissions, and only their original survey data were included in the primary analysis.

There was a balance of patients by gender: 46% were women and 54% were men (Table 2a). About 74% of the sample was in the age group of 50 to 69 years. Of the patients responding, 47 had a blood cancer diagnosis, while the others either had a solid tumor diagnosis or were unsure of their diagnosis. A further breakdown of tumor types is included in Table 2a; information on the stage of disease or treatment type was not collected.

One of the most important factors in designing this study was to assess the frequency with which our oncologists were having EOL discussions with their patients. Even though the patients were of variable ages and diagnoses, only 29% (n = 20) of the patients indicated that they had had a conversation with their oncologist regarding their EOL wishes. Women reported having this conversation slightly more often than men (35% vs 24%, $P = 0.42$), but the difference was not significant. Similarly, patients over the age of 60 reported having an EOL discussion more often than younger patients (36% vs 22%, $P = 0.29$), but again, the difference was not significant. Finally, the percentage of patients who reported having a conversation with their oncologist was not statistically different between those with a blood cancer versus a solid tumor (28% vs 33%).

Out of the 20 patients who had a discussion with their oncologist, 12 patients (60%) said they, not their doctor, initiated the discussion. As shown in Table 2b, 16 or the 20 patients (80%) agreed or strongly agreed that their treating oncologist was comfortable having a discussion on EOL issues; 3 (15%) responded neutral, and only one person strongly disagreed with this statement. None of the patients who had an EOL discussion with their oncologist felt uncomfortable having this discussion, and none were dissatisfied with the amount of time they spent having this discussion. Most patients who took the survey stated

---

Table 1. Survey items to determine factors associated with advance care planning in a hospitalized cancer population

| 1. Location/unit name |
| 2. Have you completed this questionnaire before? |
| 3. Cancer diagnosis |
| 4. Date of diagnosis (month and year) |
| 5. Gender |
| 6. Current age |
| 7. Have you ever had a discussion with your oncologist regarding your wishes when you become very ill or close to dying? |
| 8. Did they initiate it, or did you? |
| 9. My oncologist was comfortable having this discussion. |
| 10. I was comfortable having this discussion with my oncologist. |
| 11. I was satisfied with the amount of time my oncologist spent having this discussion with me. |
| 12. Have you had a discussion with any other health care provider(s) regarding your wishes when you become very ill or dying? |
| 13. How often do you visit your treating oncologist? |
| 14. How often do you visit your primary care provider? |
| 15. Describe your relationship with your treating oncologist. |
| 16. Describe your relationship with your primary care provider. |
| 17. I trust my treating oncologist. |
| 18. I trust my primary care provider. |
| 19. I am comfortable asking my treating oncologist questions regarding my care. |
| 20. I am comfortable asking my primary care provider questions regarding my care. |
| 21. My treating oncologist encourages me to ask questions related to my care. |
| 22. My primary care provider encourages me to ask questions related to my care. |
| 23. My treating oncologist explained why I was admitted to the hospital in a way I could understand. |
| 24. Do you know what a living will is? |
| 25. Do you have a living will or an advance directive? |
| 26. Please enter today’s date. |
they had a good to a very good relationship with their treating physician, and over 90% of the patients felt comfortable asking their doctors questions regarding their treatment and care. Almost all the patients said they were encouraged by their oncologist to ask questions related to their care. Interestingly, although the majority of patients (96.9%) knew what a living will was, only 53.9% had one at the time of the survey. Seventy-one percent of those who had a discussion with their oncologist also reported that they had a living will or other AD versus 48% among those who did not have a discussion with their oncologist \( (P = 0.16) \). Of those patients who had a discussion with either their oncologist or another provider, 70% stated that they had a living will, while 45% did not \( (P = 0.73) \). We did find that older patients (over 60 years) were more likely to have a living will or other AD: 67% in the over-60 group vs 40% in the <60 age group \( (P = 0.05) \). There was not a difference in the percentage having a living will based on cancer type (solid vs blood) or gender. In a multivariate logistic model, age >60 years was the only patient characteristic that was significantly associated with having a living will or AD (odds ratio 2.98; 95% confidence interval [1.02, 8.67]). No additional variables listed in Table 3 were significant in this model.

**DISCUSSION**

The results of our survey showed a slightly higher percentage of patients (54%) with an AD compared with other reports.
Various reports show that between 25% and 40% of the general population has living wills or other AD (1, 2, 4). In a study of oncology inpatients in a Virginia teaching hospital, 41% had an AD. In a study of cancer patients in a Veterans Administration Hospital, 47% had a documented AD, and 81% had some documentation in their chart that referred to their EOL preferences (8).

Our survey demonstrated a trend to a higher likelihood of having an AD for those patients who had a discussion with their oncologist and/or other health care provider. Only a minority of our patients (29%) had an EOL discussion with their oncologist, and these results were similar to the 31% reported by Zhang et al (4). In addition, patients who had a discussion with their oncologist reported feeling comfortable with the discussion and the length of the conversation. In the report of the Virginia patients, only 7% reported having an AD discussion with their oncologist; moreover, only 23% said they would like to discuss AD with their oncologist (5).

When Snyder and colleagues surveyed primary care physicians regarding their understanding of and experience with advance care planning (2), they found that only 43% reported having those discussions with the appropriate patients; 44% felt that the discussions took too much time, and most felt that the appropriate time to have the conversation was in the estimated last 6 months of life (6). The inclusion of other specialists and mid-level providers may help overcome the time constraints that some physicians face.

This study has a few limitations that must be acknowledged. As with all surveys, the findings are self-reported, and a convenience sample of patients willing to participate was used. Information on stage or current treatment was not requested. Keating et al reported that many physicians delayed EOL discussions until there was symptomatic progression and/or limited options (3). We do not have sufficient data to judge if that occurred with our patients. Our population included patients undergoing blood and marrow transplants for hematologic malignancy, patients with complications of chemotherapy, as well as patients with advanced-stage disease. In addition, our inpatient population may be quite different from that of a usual cancer outpatient population or many inpatient populations. We see a high percentage of patients with malignancies of the hematologic system, and many undergo autologous and allogeneic blood stem cell transplantation with curative intent. A smaller percentage of the patients surveyed had solid malignancies. Although no significant differences were seen between patients with hematologic versus solid tumor malignancies, we did find that a higher percentage of patients with blood malignancies had an AD. Due to the small sample size, there is a lack of statistical power for subgroup analysis for many of the comparisons presented. However, the counts and percentages are shown so readers can conclude for themselves the clinical relevance of the differences seen in this study.

Although we do not have the information, it is likely some patients in our study were admitted with end-stage disease. In the report by Mack et al, all patients had advanced solid tumor malignancies. In that study, oncologists documented EOL discussion with only 27% of their patients, but over 70% had EOL care discussions identified by at least one source (7). The percentage reporting discussions with their oncologist was similar to our findings; in contrast, in our population few of the patients reported having such a conversation with another health care provider. This may reflect differences in involvement of palliative care teams or other providers. The one factor in our population that reached statistical significance was age, with a higher percentage of those over 60 having an EOL discussion compared to the younger patients. This is consistent with trends in the general population, with the likelihood of having a living will increasing with age (1).

Unfortunately, there is little formal training available for physicians regarding EOL discussions. A study done at Duke University Medical Center involved having medical residents take part in a short intensive course to improve communication with patients at the end of their life. The group of residents who participated in the course demonstrated significant

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with a living will or advance directive*</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Had a discussion with their oncologist</td>
<td>Yes: 71% (12/17)</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>No: 48% (23/48)</td>
<td></td>
</tr>
<tr>
<td>How often visited oncologist</td>
<td>Weekly or more often: 66% (19/29)</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td>Less than weekly: 41% (11/27)</td>
<td></td>
</tr>
<tr>
<td>Had a discussion with either their oncologist or another health care provider</td>
<td>Yes: 70% (16/23)</td>
<td>0.07</td>
</tr>
<tr>
<td></td>
<td>No: 45% (19/42)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>&lt;60: 40% (13/32)</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>≥60: 67% (22/33)</td>
<td></td>
</tr>
<tr>
<td>Cancer type</td>
<td>Solid tumor: 40% (8/20)</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>Blood: 60% (27/45)</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male: 58% (21/36)</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>Female: 48% (14/29)</td>
<td></td>
</tr>
<tr>
<td>Relationship with oncologist</td>
<td>Very good: 60% (27/45)</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>&lt;Very good: 40% (8/20)</td>
<td></td>
</tr>
<tr>
<td>Relationship with primary care physician</td>
<td>Very good: 57% (17/30)</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>&lt;Very good: 51% (18/35)</td>
<td></td>
</tr>
</tbody>
</table>

*Numbers in parentheses show the number answering the question. Three individuals who answered the variable question did not answer whether or not they had a living will or advance directive.
increases in their overall skill ratings in the delivery of bad news as compared to a control group of residents, and the patients of the residents involved in the course reported greater trust in their oncologists than did the patients of control oncologists (9). Others have reported similar benefits following interventions to improve physician communication. Fallowfield et al showed that British oncologists attending a 3-day intensive communications skills seminar demonstrated significant improvement (10); similar interventions with oncology nurses also yielded positive results (11). Through interventions based on our survey findings, we hope to improve the frequency and quality of EOL discussions. Twelve domains of physicians’ skills were defined by focus groups of patients, family members of those who died with a chronic disease, and health care workers. The domains may provide a framework to focus on physicians’ skill at providing high quality EOL care (12). Such a framework presents essential skills for oncologists—both those in training and those in practice—to attain to better serve their patients.

It has been shown that in the last week of life, advanced cancer patients who reported having an EOL discussion with physicians had significantly lower health care costs. Higher costs were associated with worse quality of death (4). A recent report documented that EOL care for Medicare beneficiaries varies widely and is highly intensive, and these findings are exhibited over a wide spectrum of hospital classifications (13). Our findings indicate that more needs to be done to ensure that patients with cancer have timely discussions regarding EOL discussions and that they have understood the information provided. This will involve efforts of their oncologists as well as other members of the health care team, to include palliative care practitioners and oncology mid-level providers. Temel et al has reported that non–small cell lung cancer patients who had early palliative care consultation had a more accurate assessment of their prognosis (14). Utilizing the information gathered in this study as a baseline, further quality improvement endeavors will be developed and implemented. Specifically, we will use the information obtained in this patient survey to evaluate future efforts to improve EOL discussions and AD planning. Efforts will include implementation of programs designed to improve physicians’ communication skills around EOL discussions and greater incorporation of palliative care and other providers, including mid-level providers, to complement the oncologist’s role in providing information to patients. Even though patients who had discussions with the oncologist reported comfort on their part and that of the oncologist, this represented only 30% of the patients surveyed. The survey did not address the physician perspective, but by providing increased awareness, better tools, and additional resources, it is hoped that more oncologists will address these issues with their patients. Our philosophy is to bring all available measures to bear in order to further advance the necessary and appropriate components of advance care planning in the oncology setting.

Incidence and severity of respiratory insufficiency detected by transcutaneous carbon dioxide monitoring after cardiac surgery and intensive care unit discharge

Elaine E. Lagow, RN, CCRC, Barbara “Bobbi” Leeper, MN, RN, CCRN, Linda W. Jennings, PhD, and Michael A. E. Ramsay, MD

Patients undergoing coronary artery bypass surgery and/or heart valve surgery using a median sternotomy approach coupled with the use of cardiopulmonary bypass often experience pulmonary complications in the postoperative period. These patients are initially monitored in an intensive care unit (ICU) but after discharge from this unit to the ward they may still have compromised pulmonary function. This dysfunction may progress to significant respiratory failure that will cause the patient to return to the ICU. To investigate the severity and incidence of respiratory insufficiency once the patient has been discharged from the ICU to the ward, this study used transcutaneous carbon dioxide monitoring to determine the incidence of unrecognized inadequate ventilation in 39 patients undergoing the current standard of care. The incidence and severity of hypercarbia, hypoxia, and tachycardia in post–cardiac surgery patients during the first 24 hours after ICU discharge were found to be high, with severe episodes of each found in 38%, 79%, and 44% of patients, respectively.

Respiratory complications after cardiac surgery have been shown to result in prolonged hospital length of stays and increased costs of care (1, 2). A retrospective review of these patients at our institution demonstrated a 5% to 10% early intensive care unit (ICU) readmission rate with the main diagnosis of respiratory failure. If the patients at risk could be identified by better monitoring, perhaps an earlier intervention could be made that would prevent the need to return to the ICU and the increased costs involved. To that end, this prospective observational study analyzed the adequacy of ventilation and oxygenation by measuring transcutaneous carbon dioxide (tcpCO₂) and peripheral hemoglobin saturation (SpO₂) when the postoperative cardiac surgery patient was initially admitted to the ward from the ICU.

METHODS

Institutional review board approval was obtained at Baylor University Medical Center at Dallas to enroll patients undergoing major open cardiac surgery between October 2009 and October 2012. All patients were between the ages of 18 and 85. Patients were excluded for any prior use of an investigational device/drug within the last 30 days, any condition that would require extensive time off the nursing unit during the first 24 hours (e.g., hemodialysis), allergy to the ear probe, or an inability to undergo all protocol requirements. Prior to enrollment, all patients were screened for study eligibility and their medical history was reviewed. Informed consent was obtained preceding any study procedure, and 51 patients were enrolled.

All patients received a standard general anesthetic appropriate for cardiac surgery and were transported to the ICU immediately postoperatively. Following overnight or appropriate recovery in the ICU, patients were discharged to the cardiac telemetry ward, where they received the usual standard of care. To meet discharge criteria, all patients had to be separated from ventilatory support and require only supplemental oxygen via nasal cannula. The goals of this study were to determine the incidence of unrecognized respiratory depression during usual and customary care of these patients, and also to determine how well patients tolerated the sensor and how secure it was following placement. Therefore, the data obtained from the device were not made available to the caregivers, including both the physicians and the bedside nurse, but were recorded and reviewed later.

Upon arrival to the telemetry floor, a TOSCA 500® or TCM TOSCA® (Radiometer Medical ApS, Brønshøj, Denmark) monitor was attached to an earlobe of the patient. The TOSCA is approved by the US Food and Drug Administration for simultaneous continuous monitoring of tcpCO₂, functional oxygen saturation, and pulse rate in adults and children (Post Market Approval #K063434). The monitor provides information on both oxygen saturation and carbon dioxide levels (3–7). The tcpCO₂ reading from the TOSCA has been shown to correlate well with arterial carbon dioxide levels (PaCO₂) (8–10). The TOSCA probe is attached to the earlobe and is heated to facilitate blood flow and capillary vasodilation below the sensor. The sensor temperature may be set between 37°C and 45°C in...
steps of 0.5°C with an accuracy of ±0.2°C. The manufacturer recommends that the probe be heated to 42°C to adequately enhance blood flow, with a change in probe site every 12 hours to prevent thermal burn (9, 11). Two models of the TOSCA monitor were utilized in this study, the TOSCA 500 and the TCM TOSCA. The TOSCA 500 monitor stores all measured patient results every 3 seconds and was used earlier in the study, followed by the TCM TOSCA model, which stores all measured patient results every 10 seconds. Computer software enables data collected from the monitor to be exported to other programs. Therefore, SpO₂, tcpCO₂, and heart rate data every 3 or 10 seconds were available for analysis.

Hypercarbia for this study was classified as mild (tcpCO₂ 42–49 mm Hg), moderate (tcpCO₂ 50–59 mm Hg), or severe (tcpCO₂ ≥60 mm Hg). Hypoxia for this study was classified as mild (SpO₂ 91%–85%), moderate (SpO₂ 84%–80%), or severe (SpO₂ ≤79%). Tachycardia for this study was classified as mild (pulse rate 80–90 bpm), moderate (pulse rate 91–119 bpm), or severe (pulse rate ≥120 bpm). Events for the study were cataloged singularly into events of tcpCO₂ ≥60 mm Hg, SpO₂ saturation ≤79%, and pulse rate ≥120 bpm. Events were also cataloged with combinations of SpO₂ saturation of ≤79% with a tcpCO₂ ≥60 mm Hg; SpO₂ saturation ≤79% with a pulse rate ≥120 bpm; and SpO₂ saturation ≤79% with pulse rate ≥120 bpm plus a tcpCO₂ ≥60 mm Hg.

RESULTS

A total of 51 patients were enrolled in the study, 15 women and 36 men, with a mean age of 63 years. Forty-five of the patients were white or Hispanic and six were black. Twelve of the 51 patients were not included in the final analysis: three withdrew consent prior to the probe being applied; one was in the ICU for an extended period of time and was transferred directly to the rehabilitation hospital, bypassing the telemetry unit; and the remaining eight patients experienced machine malfunction and/or staff error. Twenty-six of the patients were attached to the TOSCA 500 for up to 24 hours from December 2009 through January 2011. Thirteen were attached to the TCM TOSCA for up to 24 hours from March 2012 through October 2012.

The total number of actual recorded hours for all 39 patients was 713 hours: 18% of patients had ≤9 hours, 31% had >9 to <20 hours, and 51% had ≥20 hours. The tcpCO₂ sensor was functional for a mean of 74% of potential recorded time. The O₂ saturation sensor was functional for a mean of 90% of this time. Twelve patients who were connected to the monitors asked to discontinue the study due to the inconvenience of the probe or annoyance with the alarm on the machine. The total time monitored in this group was 141 hours. There were three files that recorded only the first 12 hours.

One patient returned to the ICU with respiratory distress the third day after transfer to the ward. The study was designed to monitor only the first 24 hours posttransfer and therefore did not detect this event when the data were reviewed. However, the patient did exhibit periods of desaturation during the first 8 hours posttransfer, and the oxygen delivery rate was increased from 4 L per minute via nasal cannula to 5 L per minute per nursing unit protocol.

Figure 1 summarizes the number of hypercarbic, hypoxic, and tachy cardiac events, and Table 1 summarizes the duration of these events. Overall, there were 41 moderate or severe hypercarbic events. The total duration of tcpCO₂ ≥60 mm Hg was 39.03 ± 72.24 (SD) minutes, ranging from 0.05 to 280 minutes, with a median of 13 minutes. The total duration of tcpCO₂ ≥60 mm Hg was 129.6 ± 218.1 minutes, ranging from 0.05 to 1092 minutes with a median of 67 minutes. The total duration of SpO₂ saturation ≤79% in patients experiencing hypoxic episodes was 4.4 ± 9.9 minutes, ranging from 0.1 to 49.7 minutes with a median of 1.1 minute. A pulse rate

<table>
<thead>
<tr>
<th>Event</th>
<th>Number of patients with at least one event</th>
<th>Median total duration (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild hypercarbia (42–49 mm Hg)</td>
<td>35</td>
<td>303</td>
</tr>
<tr>
<td>Moderate hypercarbia (50–59 mm Hg)</td>
<td>26</td>
<td>67</td>
</tr>
<tr>
<td>Severe hypercarbia (≥60 mm Hg)</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td>Severe oxygen desaturation (≥79%)</td>
<td>31</td>
<td>1.1</td>
</tr>
<tr>
<td>Severe tachycardia (≥120 bpm)</td>
<td>17</td>
<td>3.1</td>
</tr>
</tbody>
</table>
≥120 beats/minute occurred in 17 patients, with a total duration of 11.8 ± 20.5 minutes, ranging from 0.1 to 78.0 minutes with a median of 3.1 minutes. Thirty-one percent of these tachycardic patients had a history of atrial fibrillation. As shown in Figure 2, 21% of the patients experienced all three symptoms of severe hypercarbia, hypoxia, and tachycardia in the first 24 hours after discharge from the ICU.

**DISCUSSION**

We presented results of 39 postoperative cardiac surgery patients during their first 24 hours following transfer from the ICU to the telemetry floor, showing that the incidence and severity of hypercarbia, hypoxia, and tachycardia were high. The continuous monitoring of tcpCO2, SpO2, and pulse rate provides earlier identification of severe respiratory depression, and therefore would lead to earlier intervention and possibly prevent a return to the ICU. Monitoring is particularly important for patients with a history of pulmonary disease, which may increase postoperative complications and ICU stay. A well-tolerated patient monitoring technology that accurately, automatically, and continuously tracks transcutaneous carbon dioxide levels has the potential to greatly improve the timeliness of a response to a failing patient and improve patient safety and outcomes. The episodes of severe hypoxia, hypercarbia, and tachycardia detected in this study indicate a need for improved monitoring of this patient population.

There were several limitations to our study. First, although 51 patients agreed to participate, we were able to analyze data for only 39 patients. Of those 39, approximately 76% of potential monitored hours were captured. The study monitor TOSCA 500 was upgraded to the TCM TOSCA during the trial. Several patients asked to have the monitor removed early due to continued alarming and comfort level being restricted due to “one more wire” being attached to them. The monitor may have been better tolerated by patients if it were wireless. Some of the technical problems encountered may have been avoided with better education for the nursing staff.

The clinical significance of our findings will need to be determined by a larger study, where the monitor information is provided to the nurses and an intervention protocol put in place. Monitoring tcpCO2, SpO2, and pulse rate through a single sensor could provide an advantageous and convenient method of early detection of potential severe respiratory depression.

**Acknowledgments**

Funding for this study was wholly provided by the Cardiovascular Research Foundation of the Baylor Heart and Vascular Institute. The monitors were provided by Radiometer (Brønshøj, Denmark).

Outcome assessment of 603 cases of concomitant inferior turbinectomy and Le Fort I osteotomy

Reza Movahed, DMD, Carlos Morales-Ryan, DDS, MSD, Will R. Allen, DDS, Scott Warren, DDS, MD, and Larry M. Wolford, DMD

This retrospective study assessed the outcome of 603 patients undergoing partial inferior turbinectomies (PIT) in association with Le Fort I osteotomy. The study included 1234 patients from a single private practice; these patients had dentofacial deformities and underwent Le Fort I osteotomy procedures. For the full patient group, 888 patients (72%) were women; in the turbinectomy group, 403 (67%) were women. The anteroposterior, transverse, and vertical dimensions of the mandible, maxilla, and occlusal plane of each subject were assessed, in addition to cephalometric analysis and determination of the presence or absence of temporomandibular joint disorders. PIT, when indicated, was performed after downfracture of the maxilla, providing access to the turbinates where approximately two thirds of the total turbinate volume was removed and septoplasty was completed if indicated. Hypertrophied turbinates causing significant nasal airway obstruction were present in 603 (49%) of the 1234 patients undergoing Le Fort I osteotomy. The results of this study showed that PIT performed simultaneously with Le Fort I osteotomy is a safe method of managing nasal airway obstruction related to hypertrophied turbinates with minimal complications.

The nasal turbinates or conchae are curled thin bone shelves that protrude from the lateral nasal walls medially into the nasal breathing passage covered with glandular, erectile, and mucosal tissues. Three turbinates are arranged in horizontal parallel rows on each side of the nose. The inferior turbinate is the largest, followed by the middle, and the superior turbinate is the smallest. The turbinates divide the nasal airway into four air passages, which guide the inhaled air to flow in a steady stream around the largest possible surface of cilia. In the presence of normal anatomy, the inferior turbinates play a major role in filtering, warming, and humidifying the nasal airway, with approximately 80% of the airflow occurring around the inferior turbinates. The sympathetic and parasympathetic nervous systems are responsible for change in the turbinate size according to physiologic requirements (1). This is a cyclical set of events, which is affected by increasing or decreasing the volume of blood contained in the associated erectile tissue.

Large or swollen turbinates may lead to decreased air flow through the nasal passage. Allergic exposure to environmental elements and allergens, in addition to persistent inflammation within the sinuses, can lead to turbinate swelling. Anatomical and traumatic factors can also play a role in this process. Deformed and enlarged inferior turbinates are the main causes of nasal airway obstruction, followed by allergic rhinitis (2, 3). Epidemiologic studies in European countries have shown that up to 20% of the population has chronic nasal obstruction caused by turbinate hypertrophy (4). The most common causes of hypertrophied turbinates are allergic and nonallergic nasal hyperactivity, followed by septal deviation (5). The sequel of chronic nasal obstruction is mouth breathing, which results in a lower and anteriorly placed tongue and a lower position of the mandible. This consequently decreases the tonicity of the facial muscles as a result of decreased flow of the nasal airway due to anatomical obstruction (6–8). Based on functional matrix theory, put forth by Moss et al (9), the lack of nasal breathing can significantly affect the development of dentofacial and craniofacial structures. In an individual with obstructed nasal airway, disharmony of normal breathing and abnormal tone and stimulation of facial muscles could be the cause of a narrow and posteriorly positioned mandible, in addition to a hypoplastic maxilla, associated with open bite (10–12).

The allergic turbinate hypertrophy can be managed with medications, such as corticosteroids, and if this approach fails, surgery may be necessary (13). When a deviated septum is identified, the turbinate associated with the affected side is usually enlarged. In such cases, the septum can be addressed along with the enlarged turbinate. Chronic nasal stuffiness, caused by perennial allergic rhinitis, is amenable to turbinate surgery (14).

Multiple surgical modalities have been advocated to address the hypertrophied turbinate, including turbinate outfracture, electrocautery, reduction by a microdebrider, cryosurgery, coablation, laser reduction, partial or total turbinate resection, use of radiofrequency, submucous turbinate resection, and vidian neurectomy (13, 15–19). The aim of this retrospective study was to perform an outcome assessment of partial inferior turbinectomies (PIT) performed simultaneously with Le Fort I osteotomies and analyze the related data for complications, gender...
distribution, and morphological association with the maxilla and mandible.

METHODS

A retrospective study was conducted on 1234 consecutive patients (888 women, 346 men) from the senior author’s (Wolford) private practice (Dallas, Texas) undergoing Le Fort I osteotomy from 1995 to 2011. These patients required Le Fort I osteotomies for correction of dentofacial deformities, and a significant number of patients also required temporomandibular joint (TMJ) surgery. Institutional review board exemption was obtained.

The surgical technique for PIT was as follows. In the maxillary osteotomies, prior to mobilization, the nasal mucosa was carefully dissected off the nasal floor, the lateral nasal wall up to the base of the inferior turbinate, and off the inferior aspect of the nasal septum. The septum was separated from the maxillary nasal crest. The maxilla was downfractured and mobilized, with care taken to preserve the nasal mucosa intact. Using a 15 blade, an incision was made bilaterally, just lateral to the septum, extending from the posterior to the anterior aspect of the nose. Retracting the mucosal tissue laterally exposed the entire body of the turbinates (Figure 1a). The portion of the turbinates to be resected was isolated and excised using scissors (Figure 1b). Hemostasis was achieved using a Bovie cautery. If a nasoseptoplasty was indicated, the mucosa was dissected off the septum and an appropriate procedure performed to correct the septal deformity. The nasal mucosa was approximated using 4.0 chromic gut sutures in a running fashion, incorporating all four mucosal flaps. Postsurgical imaging on a typical patient demonstrated the reduced turbinates (Figure 2c, 2d).

There were three diagnostic criteria for hypertrophic turbinate: 1) a history of consistent difficulty breathing through the nose; 2) clinical and radiographic evidence of the turbinate blocking the majority of the nasal airway; and 3) predominant mouth breathing when sleeping. Evaluations included medical history; clinical assessment; standardized x-rays; dental models; clinical pictures; morphological evaluation of maxilla, mandible, and occlusal plane angle; evaluation of external and internal nasal deformities; and determination of any current respiratory problems. In cases prior to 2008, radiographic images were obtained with the Quint Sectograph, and after 2008 with cone beam computed tomography (CT) scan. These radiographs were taken in the normal course of patient treatment.

Lateral cephalograms, anteroposterior radiographs, and cone beam CT scans were analyzed to determine the transverse, vertical, and anteroposterior dimensions of the maxilla and mandible as well as the occlusal plane angle. The maxilla and mandible were categorized into hypoplastic, hyperplastic, and normal groups. The occlusal plane angle was labeled as normal, low, or high angle.

The total patient group (n = 1234) was also evaluated for the presence of and correlation between hyperplastic turbinates and TMJ surgery. The TMJ surgeries performed included TMJ disc repositioning using the Mitek anchor technique (Mitek Inc, Norwood, MA) and TMJ reconstruction using TMJ Concepts (Ventura, CA) total joint prostheses. The gender variation and correlation to PIT were evaluated. Descriptive statistics and Pearson’s correlation analysis were utilized to evaluate the results.

RESULTS

Among the 1234 patients enrolled in the study, 888 (72%) were women, and 346 (28%) were men. In 603 cases (49%), partial turbinectomies were required. In this subgroup, 403 (67%) were women and 200 (33%) were men. In 603 cases (49%), partial turbinectomies were required. In this subgroup, 403 (67%) were women and 200 (33%) were men. In 603 cases (49%), partial turbinectomies were required. In this subgroup, 403 (67%) were women and 200 (33%) were men. In 603 cases (49%), partial turbinectomies were required. In this subgroup, 403 (67%) were women and 200 (33%) were men. In 603 cases (49%), partial turbinectomies were required. In this subgroup, 403 (67%) were women and 200 (33%) were men. In 603 cases (49%), partial turbinectomies were required. In this subgroup, 403 (67%) were women and 200 (33%) were men. In 603 cases (49%), partial turbinectomies were required. In this subgroup, 403 (67%) were women and 200 (33%) were men.

Of the 603 patients, 296 (49%)—including 215 (73%) women and 81 (27%) men—received concomitant TMJ surgery, Lefort I osteotomy, and PIT. The remaining 307 patients—188
(61%) women and 119 (39%) men—received PIT and Lefort I osteotomy with no TMJ surgical intervention (Table 1).

All the patients were followed immediately postoperatively and at long-term follow-up of 12 to 48 months. Chart review showed no significant long-term complications associated with PIT.

DISCUSSION

Hypertrophied turbinates can be addressed with various means, from conservative therapy (20) to surgical modalities. In

---

**Table 1. Patient gender by procedure**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lefort I osteotomy and PIT (N = 603)</td>
<td>200 (33%)</td>
<td>403 (67%)</td>
</tr>
<tr>
<td>Subgroup with no TMJ surgery (N = 307)</td>
<td>119 (39%)</td>
<td>188 (61%)</td>
</tr>
<tr>
<td>Subgroup with TMJ surgery (N = 296)</td>
<td>81 (27%)</td>
<td>215 (73%)</td>
</tr>
</tbody>
</table>

PIT indicates partial inferior turbinectomies; TMJ, temporomandibular joint.

---

**Table 2. Skeletal morphological characteristics that correlate with turbinate hyperplasia**

<table>
<thead>
<tr>
<th></th>
<th>Anteroposterior</th>
<th>Vertical</th>
<th>Transverse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maxilla</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>12%</td>
<td>13%</td>
<td>45%</td>
</tr>
<tr>
<td>Hypoplasia</td>
<td>84%*</td>
<td>48%</td>
<td>52%</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>4%</td>
<td>39%</td>
<td>3%</td>
</tr>
<tr>
<td>Mandible</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>10%</td>
<td>95%</td>
<td>98%</td>
</tr>
<tr>
<td>Hypoplasia</td>
<td>72%*</td>
<td>2.5%</td>
<td>0.8%</td>
</tr>
<tr>
<td>Hyperplasia</td>
<td>18%</td>
<td>2.5%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Occlusal plane</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>27%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>4%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>69%*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*P ≤ 0.05.

---

Figure 2. Computed tomography scans of a typical patient before and after the procedure. (a) Axial view demonstrates hypertrophied turbinates (arrows) and the nasal septum that appears reasonably straight. (b) Coronal view demonstrates hypertrophied turbinates (arrow) occupying the majority of the nasal cavity. (c) After turbinectomy, along with the maxillary osteotomies, the axial view shows the patient’s improved nasal airway. The cut is just inferior to the remaining turbinates. (d) Coronal view shows the reduced turbinates and improved nasal airway.
patients with dentofacial deformities, the Le Fort I osteotomy provides direct access to the full extent of the inferior turbinates and the septum. The patients in this study with hypertrophied turbinates were treated with PIT in combination with maxillary and mandibular ostetomies with correction of the occlusal plane to a normal angulation as well as TMJ surgery when indicated to provide optimal function, facial balance, decrease in pain, and good airway (Figure 3d–3f, 4d–4f, 5b). A female predominance was seen in the data reviewed. Approximately 67% of the turbinectomy cases, and 73% of concomitant turbinectomy and TMJ surgery cases, involved female subjects. A strong correlation has been established between hypertrophied inferior turbinates, hypoplastic maxilla and mandible, as well as a steep occlusal plane. Our findings correlate with other studies evaluating the morphology of mouth breathing and nasally obstructed patients (6, 21–23).

The association of mouth breathing, dentofacial deformities, and upper airway obstruction has been explored in the orthodontic, otolaryngology, and maxillofacial surgery literature (24). It still remains a controversial subject with no general consensus achieved (25–28). Harvold et al (29), in their primate studies, induced obstruction of the nasal airway and generated morphological changes in dental and craniofacial parameters. McNamara (30) proposed a physiological mechanism that describes the association of upper respiratory obstruction and changes in the neuromuscular system that alters the bony, soft tissue, craniofacial, and dental structures.

When addressing hypertrophied turbinates along with correction of dentofacial deformities, especially in the case of performing Le Fort I osteotomies, postsurgical patency of the airway should be considered (31–33). When the Le Fort osteotomy is performed, the maxilla can be mobilized, repositioned, and stabilized in any of four possible directions, affecting the associated and adjunctive soft tissues (34). In 1997 Kunkel and Hochban (35) utilized the acoustic rhinometry concept introduced by Hilberg et al in 1989 (36) to evaluate the effect of maxillary movement on the nasal volume. Erbe et al in 2001 completed acoustic and rhinometry evaluation of 21 maxillary advancement and impaction cases and concluded that in anterior and superior maxillary repositioning, there was no significant change in airflow resistance (37). Haarmann et al (2009) investigated the changes in nasal airways after Le Fort I osteotomies with concomitant nasal septoplasty and inferior turbinectomies using anterior rhinomanometry and acoustic rhinometry. The results of their analysis supported the improvement of the functional airway after surgery (38).

The simultaneous reduction of inferior turbinates is of importance in cases requiring maxillary superior repositioning for management of upper airway obstruction in the presence of hypertrophied turbinates. Multiple publications have addressed and reported case series on the subject (38–40).

In the reviewed sample size (n = 603), no significant long-term postsurgical complications related to the nasal airway were identified. The most common complications from turbinate surgery are hemorrhage, atrophic rhinitis, and ozena (41). The reduction of the appropriate volume of the inferior turbinate is of importance, taking into account the presented histological factors and maintenance of mucociliary function. The resection of the entire turbinate increases the patency of the nasal airway but increases the chance of intraoperative and postoperative heavy bleeding, while having a long-term chance of chronic nasal crusting (42–44).

Presently there is no exact consensus on the volume of reduction or the method utilized for PIT. Based on this case series, clinical outcomes, and preservation of the function of the nose, the recommended reduction of the hypertrophied inferior turbinates should equal about two thirds of the original volume.
Excessive reduction of turbinate tissue could cause the rare empty nose syndrome (ENS). ENS is associated with poor regrowth of sensory nerves, which are damaged during aggressive turbinectomies. In ENS, the nasal airway is unobstructed, but the affected patients sense an unsatisfactory struggle to breathe (48, 49). Ear, nose, and throat specialists presently believe that ENS is a diagnosis with no criteria for its identification and in general recommend conservative reduction of the turbinates for its prevention (50).

In conclusion, PIT is a predictable and safe procedure performed simultaneously with Lefort I osteotomy for patients identified with hypertrophic inferior turbinates and nasal airway obstruction. A notable pattern was established in our patient population, which clinically associates female patients with high occlusal plane, hypoplastic maxilla, and mandible complex as the predictable group for hyperplastic turbinates requiring PIT. In assessing this study, it is important to understand that most patients associated with the senior author's practice are retrognathic patients, with associated TMJ disorders, which could have an effect on the patient sample. The relation between TMJ disorders and hypertrophied turbinates is also noteworthy, and a larger multicenter controlled group will be necessary for establishing its implication. Our recommendation is that in patients with dentofacial deformity undergoing Le Fort I osteotomy, the general status of the patients' breathing and nasal structures should be taken into consideration for concomitant surgical intervention.

8. Valera FC, Travitzki LV, Mattar SE, Matsumoto MA, Elias AM, Anselmo-Lima WT. Muscular, functional and orthodontic changes in pre school


Copper deficiency (hypocupremia) and pancytopenia late after gastric bypass surgery

Sara D. Robinson, MD, Barry Cooper, MD, and Temekka V. Leday, MD, PhD

Hypocupremia, or copper deficiency, is a rare and underrecognized cause of bone marrow dysplasia. Most cases of copper deficiency in adults occurred historically in patients receiving total parenteral hyperalimentation or total parental nutrition. More recently, with the obesity epidemic and the prevalence of gastric bypass, cases of malabsorption-related copper deficiency have occurred. Copper deficiency can lead to significant cytopenias and possible neurologic sequelae, which can be misdiagnosed and mismanaged. Unfortunately, a delay in diagnosis and appropriate treatment may lead to permanent neurologic damage. We describe a woman with previous gastric bypass surgery who presented with pancytopenia and bone marrow biopsy findings consistent with a myelodysplastic syndrome with excess blasts. She was found to be significantly copper deficient. With replacement copper therapy, her cytopenias quickly resolved. We discuss the distinctive clinical and hematologic features of this rare cause of significant cytopenias and provide recommendations for monitoring and treatment of such patients. Moreover, this case is an important reminder that bariatric patients should have routine follow-ups after surgery and continue dietary supplements indefinitely.

Copper deficiency is exceedingly rare in the normal population. Historically, most cases of copper deficiency in adults occurred in patients receiving total parenteral hyperalimentation or total parental nutrition (TPN) (1). However, after bariatric surgery, copper supply is critical, as it appears to be required for the absorption and utilization of iron, already known to be malabsorbed in this setting. Copper is present in a number of metalloproteins, and it is required as a cofactor in many redox reactions. More than 90% of copper is bound to ceruloplasmin, an α2-globulin with ferroxidase activity. The copper-dependent ferroxidase hephaestin converts iron to the ferric (Fe3+) state for its transport by transferrin (2). There is an increasing recognition of hypocupremia associated with anemia as a complication following TPN and bariatric surgery, specifically in the case of gastric resection or bariatric gastric reduction surgery (3). One characteristic associated with copper deficiency is an anemia that is unresponsive to iron supplementation but may present with pancytopenias and features of myelodysplastic syndrome (MDS). We report such a patient, discuss the distinctive clinical and hematologic features of this rarity, and provide recommendations for monitoring and treatment.

CASE PRESENTATION

A 51-year-old Caucasian woman presented to our outpatient clinic for evaluation of pancytopenia. In July 2012, a complete blood count was performed (Table 1). Her hematocrit was 33.2%, white blood cell count was 5.5 K/μL, and platelet count was 207 K/μL. In September 2012, reevaluation revealed worsening of the pancytopenia (Table 1). She received a transfusion of packed red blood cells and her hematocrit increased, but the effect was transient. At this point, the patient was referred to our office, where we performed a bone marrow biopsy. The aspirate revealed a hypercellular marrow with a mild increase in blasts (5%–6%) and trilineage dyspoiesis, morphologic findings consistent with refractory anemia with excess blasts (RAEB-1).

In taking the patient’s history, we found that she had undergone a gastric bypass procedure 20 years earlier. On her first visit to our office, her weight was 200 pounds (body mass index 34.1 kg/m2). She had diffuse musculoskeletal pain related to fibromyalgia. Since the bypass, she was taking oral iron for anemia. She was prescribed lithium for bipolar disorder and had been taking it for 6 years. She had no neurologic complaints, and she denied any excess tobacco or alcohol use. She took clonazepam, pregabalin, vitamin B12, furosemide, promethazine, tramadol, an oral multivitamin, and vitamin D. At the time of her visit to our office in October 2012, her hematocrit was 30.2%; white blood cell count, 3.8 K/μL; and platelet count, 138 K/μL. Her lactate dehydrogenase was 134 IU/L, antinuclear antibody was nonreactive, ferritin was 354 ng/mL, and reticulocyte count was 3.1%.

The peripheral blood smear demonstrated pancytopenia with marked changes in red blood cells (Figure 1). There was a normochromic, normocytic anemia with marked anisopikilocytosis that included occasional ovalocytes and dacryocytes. A distinct dimorphic red blood cell population was not evident. Among the leukocytes, there was neutropenia with relative eosinophilia. White blood cells were morphologically normal.
Platelets were mildly decreased in number with occasional large platelets present. Bone marrow aspirate smears contained scattered small particles with cellular marrow (Figure 2). There was left-shifted granulocytic maturation with increased numbers of blasts (4%–6%) and promyelocytes. Morphologically, blasts were typical of myeloid blasts. Auer rods were not present. Features of dysgranulopoiesis included asynchronous maturation and occasional hyposegmentation of neutrophils. Many of the early granulocytic precursors (blasts and promyelocytes) contained multiple small cytoplasmic vacuoles. The erythroid lineage demonstrated left-shifted maturation with increased numbers of pronormoblasts and basophilic normoblasts, many of which contained multiple small cytoplasmic vacuoles. There were mild megaloblastoid changes and dyserythropoietic changes to include nuclear irregularities, nuclear lobulation, and nuclear fragmentation. The myeloid to erythroid ratio demonstrated a slight erythroid predominance at 1.7:1. Megakaryocytes were adequate in number with occasional dyspoietic forms. Prussian blue–stained aspirate smears showed mildly increased iron stores with storage iron and sideroblastic iron identified. Ringed sideroblasts were not observed.

The core biopsy specimen demonstrated a hypercellular marrow for the patient’s age (70%)–80% with all lineages represented (Figure 3). The biopsy contained scattered immature cells. Megakaryocytes were adequate for cellularity, with focal clusters and occasional dyspoietic forms to include hypolobate and hyperlobate nuclei (Figure 3). A reticulin stain showed mildly to moderately increased reticulin fibrosis.

Flow cytometry studies performed on the bone marrow aspirate found increased eosinophils (19%) with no increase in myeloblasts (3%) or hematogones (2%). Cytogenetic analysis of the bone marrow aspirate was performed and an MDS fluorescence in situ hybridization (FISH) panel was found to be negative for deletions of chromosome loci 5q31, 7q31, and 20q, with no evidence of monosomy 7 or trisomy 8. FISH for a core binding factor subunit β rearrangement was negative. Chromosome analysis revealed a normal 46,XX female karyotype.

Given the bone marrow morphologic findings, MDS was strongly considered, although the patient was young for this diagnosis (median age 70) and had normal marrow cytogenetics. We also considered drug-induced cytopenias, with lithium or pregabalin considered the most likely inciting substances. However, lithium is generally associated with a leukocytosis, and pregabalin most commonly causes thrombocytopenia rather than pancytopenia. Nonetheless, these drugs were stopped. Given her history of bariatric surgery, which can have malabsorption–related complications, we checked her copper and zinc levels. The latter was within normal limits; however, the patient’s copper level was extremely low (<20 mcg/dL; reference range 70–175 mcg/dL), so we initiated therapy with copper gluconate 4 mg orally three times a day. Two weeks later, her white count had improved, and approximately 6 weeks after initiation of copper replacement therapy, our patient’s complete blood count had normalized (Table 1). Her copper level had risen from <20 to 101 mcg/dL. She resumed lithium and her blood counts remained normal.

**DISCUSSION**

MDS is characterized by ineffective hematopoiesis and functional abnormalities of hematopoietic lineages. In about one third of patients, this disease can transform into acute myeloid leukemia. The World Health Organization classification of MDS, updated in 2008, indicates that the features that define MDS include blood cytopenias, ineffective hematopoiesis, dysfunctional megakaryocytes, and hypercellular bone marrow. The copper deficiency hypothesis suggested that copper deficiency may play a role in the pathogenesis of MDS, particularly in patients with atypical features or early presentation.

<table>
<thead>
<tr>
<th>Table 1. Complete blood cell counts and plasma copper levels in our patient over time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
</tr>
<tr>
<td>White blood cells (K/uL)</td>
</tr>
<tr>
<td>Neutrophils (%)</td>
</tr>
<tr>
<td>Bands (%)</td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
</tr>
<tr>
<td>Monocytes (%)</td>
</tr>
<tr>
<td>Eosinophils (%)</td>
</tr>
<tr>
<td>Basophils (%)</td>
</tr>
<tr>
<td>Platelets (K/uL)</td>
</tr>
<tr>
<td>Plasma copper (mcg/dL)</td>
</tr>
</tbody>
</table>

**Figure 1.** Peripheral blood smear with pancytopenia and anisopoikilocytosis of the red blood cells (Wright, ×400).
dyserythropoiesis, dysgranulopoiesis, dysmegakaryopoiesis, and increased myeloblasts (4). RAEB-1 is defined by cytopenias with unilineage or multilineage dysplasia and 5% to 9% blasts in bone marrow or 2% to 4% blasts in the peripheral blood. RAEB-1 is considered an intermediate-risk subtype of MDS. In the absence of specific cytogenetic abnormalities, MDS is a diagnosis of exclusion, and the diagnosis should only be made after careful review of clinical history and elimination of environmental or other nonclonal disorders that can result in myelodysplasia. Congenital diseases and other enzyme deficiencies are known to demonstrate myelodysplastic changes in a single lineage; however, trilineage dysplasia is unlikely in these entities. Substances with toxic effects such as chloramphenicol or arsenic can lead to dysplasia in all cell lines.

Copper deficiency has been reported to result in an MDS-like picture. Patients often present with anemia, neutropenia, and, less commonly, thrombocytopenia (1, 5). Copper is present in a number of metalloproteins that are vital for normal homeostasis and include such enzymes as cytochrome-c oxidase, dopamine β-hydroxylase, and superoxide dismutase. It is unclear how copper deficiency causes anemia and other cytopenias. A decrease in the copper-dependent enzymes (ceruloplasmin and cytochrome-c) that aid in iron metabolism and transportation has been proposed as a potential factor for anemia (6). Mitochondria from copper-deficient animals are deficient in cytochrome oxidase activity and fail to synthesize heme from ferric iron and protoporphyrin at the normal rate, leading to mitochondrial iron accumulation (7, 8). The mechanism underlying neutropenia in hypocupremia remains unknown. Suggested etiologies have included destruction of myeloid progenitor cells in the bone marrow, inhibition of differentiation and self-renewal of CD34+ hematopoietic progenitor cells, impaired egress of neutrophils from the bone marrow, and increased clearance of neutrophils from the circulation (9, 10).

The anemia of copper deficiency often is associated with the presence of ringed sideroblasts and occurs in a number of clinical settings, including a microcytic, macrocytic, or normocytic anemia. Marked vacuolization of both erythroid and myeloid precursors has been consistently reported in bone marrow (1–7, 11). Megaloblastic changes, ringed sideroblasts, and multilineage dyspoiesis characteristic of MDS have been described (3, 10–13). In comparison, our patient’s bone marrow had numerous myeloid and erythroid precursors with cytoplasmic vacuolization, but lacked ringed sideroblasts. Of note, our patient’s bone marrow demonstrated increased numbers of myeloblasts (4%–6%) with trilineage dysplasia, suggesting RAEB-1. A case report described a 19-year-old man with intestinal amyloid and secondary copper deficiency that presented with trilineage dysplasia and increased numbers of immature cells, up to 19% (13). Though originally interpreted as blasts morphologically consistent with lymphoblasts, the immature cells in question turned out to be hematogones, or B lymphocyte precursors. Hematogone hyperplasia has been described in association with copper deficiency secondary to zinc excess, with bone marrow findings that overlap with MDS (13, 14). Sixteen patients were reported with copper deficiency over a 5-year period, 94% of which had hematologic features as their initial manifestation. Of the seven patients who had a bone marrow biopsy done, only one had an appearance consistent with RAEB-1 (15).

Figure 2. Morphologic changes in marrow precursors in copper deficiency, some of which mimic a myelodysplastic syndrome. (a) Early myeloid and erythroid precursors with cytoplasmic vacuoles (Wright, ×1000). (b) Myeloid blast and vacuolated early erythroid precursors (Wright, ×1000). (c) Megaloblastoid change and dyspoiesis in late-stage erythroid precursors (Wright, ×1000). (d) Dyspoietic ring neutrophil and vacuolated promyelocyte (Wright, ×1000).
Gastric surgery seems to be an increasingly common cause of acquired copper deficiency that can go unrecognized for years (16). Acquired copper deficiency can cause a myelopathy in humans (17) and is usually accompanied by the more typical anemia and leukopenia. Spinal and peripheral nerve injury can occur; patients can present with subacute gait disorders and prominent sensory ataxia and/or spasticity. Magnetic resonance imaging shows subcortical white matter changes, atrophy of the cerebellum, as well as signal changes in dorsal columns (15)—neurologic deficits similar to those of vitamin B12 deficiency. Though copper supplementation generally prevents further neurologic deterioration, improvement in neurologic symptoms with treatment is variable (18, 19). It is unclear if our patient’s history of fibromyalgia or diffuse musculoskeletal pain was related to her copper deficiency. She had no focal neurologic deficits at the time of initial examination, and musculoskeletal symptoms persisted after copper repletion.

Copper is an essential trace element absorbed in the stomach and proximal duodenum, both of which can be altered in bariatric surgery. Unfortunately, there have been no studies addressing the appropriate dose, duration, or form of copper supplementation, nor are there specific guidelines for replacing low serum copper. Commonly used salts include copper gluconate, copper sulfate, and copper chloride. Because of the need for long-term therapy, parenteral therapy is not recommended, although intravenous copper can be used for several days as a bridge to the oral form. A 60-year-old man with early onset copper deficiency after Roux-en-Y surgery was supplemented daily with 4 to 10 mg of oral copper (20). Monitoring the patient’s blood copper levels every few months for the first year to confirm normal serum levels is important to establish the appropriate dose. Our case is an important reminder that bariatric patients should have routine follow-ups after surgery and continue dietary supplements indefinitely. Abnormalities on routine laboratory tests should prompt a search for vitamin and trace mineral deficiencies, as early detection can prevent debilitating symptoms.


Figure 3. Hypercellular marrow for age with occasional dyspoietic megakaryocytes. (a) Hypercellular marrow particle with all lineages represented (hematoxylin and eosin, ×200). (b, c) Dyspoietic changes in megakaryocytes (hematoxylin and eosin, ×600).


---

### Avocations

A lilac breasted roller from Botswana. Photo copyright © Jed Rosenthal, MD. Dr. Rosenthal is a cardiologist in Dallas, Texas (e-mail: jedr2@sbcglobal.net).
Isolated atrial amyloidosis and the importance of molecular classification

Varsha Podduturi, MD, Danielle R. Armstrong, DO, Michael A. Hitchcock, MD, William C. Roberts, MD, and Joseph M. Guileyardo, MD

Amyloid is identified microscopically as an amorphous extracellular hyaline material that exhibits “apple-green” birefringence with Congo red stains. Amyloid is not a chemically distinct entity, and currently available molecular methods are capable of identifying over 20 amyloidogenic precursor proteins. Some of the more common diseases associated with amyloidosis include plasma cell dyscrasias, chronic inflammatory disorders, hereditary-familial mutations involving transthyretin, Alzheimer’s disease, and so-called “senile” or age-related amyloidosis. The amyloid deposits in these various diseases may be isolated to a single organ such as the heart or brain, or the amyloidosis may be systemic. The senile types of cardiac amyloidosis can result from overproduction of atrial natriuretic factor or from accumulation of otherwise normal or wild-type transthyretin. We present the case of an 83-year-old hospitalized woman with known atrial fibrillation and previous pacemaker implantation who had cardiac arrest unresponsive to attempted resuscitation. Autopsy disclosed prominent amyloidosis involving the left atrium, and subsequent molecular studies identified the amyloidogenic material as alpha atrial natriuretic factor. Since the clinical management and genetic implications of the various diseases associated with amyloidosis are markedly different, we stress the importance of molecular classification whenever possible.

Although identified microscopically as an extracellular amorphous eosinophilic material with “apple-green” birefringence by Congo red staining, amyloid is not a chemically distinct entity (1). Furthermore, the tissue distribution of amyloid among the various subtypes may be systemic or isolated to a single organ such as the heart or brain, producing completely different clinical syndromes. The more common disorders associated with amyloid deposition include immunocyte or plasma cell dyscrasias, chronic inflammatory disorders, genetic (familial) disorders, Alzheimer’s dementia, and so-called “senile” or age-related amyloid deposition. Also, within the “senile” amyloidosis category, involvement may be systemic or isolated to the heart, and two distinct subtypes of senile cardiac amyloidosis have been described. In isolated atrial amyloidosis (IAA), amyloid accumulates due to an overproduction of alpha-atrial natriuretic factor or protein (alpha-ANF, alpha-ANP) (2), whereas in senile systemic amyloidosis, the amyloid is derived from native or wild-type transthyretin, a transport protein produced by the liver (3). Since amyloidosis may cause abnormal cardiac function, including restrictive heart disease, conduction disorders, arrhythmias, and death, the clinical diagnosis and pathologic identification of this disorder are important (1). Furthermore, amyloid subtyping may inform therapy, and molecular typing may have profound implications for family members (4).

CASE STUDY

An 83-year-old woman was admitted to Baylor University Medical Center at Dallas with new-onset dyspnea and bilateral pulmonary infiltrates on chest radiograph. In the past a pacemaker had been implanted for “permanent” atrial fibrillation, and she was on warfarin with a recorded international normalized ratio of 4.4. Also, she was a long-term rehabilitation facility resident, and her problems included osteoarthritis, a hip fracture a year earlier, and poor mobility. On examination there was lower-extremity edema and muscle weakness, and she fatigued quickly. Her body mass index was 21.4 kg/m².

The patient was admitted to the telemetry floor and given diuretics. The night of admission, acute hypercapnic respiratory failure prompted admission to the intensive care unit, and bilevel positive airway pressure support was initiated. Her blood pressure was 130/70 mm Hg; heart rate, 75 beats/minute; and respiratory rate, 34 breaths per minute. A grade 2/6 holosystolic murmur was audible at the cardiac apex. Computed tomographic examination of the chest disclosed right atrial enlargement, biapical pulmonary opacities (pneumonia versus edema), and pleural effusions (left > right). A brain natriuretic peptide was 314 pg/mL (normal ≤100 pg/mL), and an alanine transaminase was 67 U/L (normal 9–60 U/L). Troponin I was 0.03 ng/mL (normal <0.05 ng/mL). Transthoracic echocardiogram disclosed a normal left ventricular cavity size and normal systolic function with an ejection fraction of 55%; a dilated right atrium and right ventricle with preserved right ventricular systolic function; mild to moderate tricuspid regurgitation; an estimated right ventricular systolic pressure of 46 mm Hg; a dilated left atrium; mild aortic regurgitation; and a small pericardial effusion.

From the Department of Pathology, Baylor University Medical Center at Dallas. Corresponding author: Joseph M. Guileyardo, MD, Department of Pathology, Baylor University Medical Center at Dallas, 3500 Gaston Avenue, Dallas, TX 75246 (e-mail: Joseph.Guileyardo@BaylorHealth.edu).
Shortly after intubation and placement of a central line, she developed ventricular fibrillation and pulseless electrical activity and died.

At necropsy, the pericardial sac contained 100 mL of clear fluid. The pacemaker leads were well seated. The heart weighed 460 g. The subepicardial adipose tissue was markedly increased, causing flotation of the heart in formalin. The epicardial surface was smooth and devoid of adhesions. The heart was examined through parasagittal incisions after fixation. The left atrial appendage was markedly dilated. Both atrial cavities were quite large and roughly dilated to similar degrees. Brown discolorations were present in the left atrial endocardium (Figure 1). The right ventricular cavity and the coronary sinus were dilated.

Microscopically, there were amyloid deposits within the walls of both atria (confirmed by Congo red stains), but these deposits were much more prominent within the left atrial wall (Figure 2). Congo red stains of the ventricular walls were negative.

CD138 immunostain and kappa and lambda in situ hybridization studies of the spinal bone marrow did not reveal plasma cytosis or cellular clonality. Postmortem serum immunofixation electrophoresis was also negative for monoclonal peaks.

To further characterize the amyloid deposits, paraffin blocks were submitted to the Mayo Clinic Laboratories, where molecular amyloid subtyping by liquid chromatography-tandem mass spectrometry was performed on peptides extracted from Congo red–positive/microdissected areas of paraffin-embedded left atrial tissue. The resultant diagnosis was amyloidosis, atrial natriuretic factor type, in the left atrium of the heart.

The remainder of the autopsy revealed moderate cerebral and aortic atherosclerosis, centrlobular hepatic congestion, mild arteriolar nephrosclerosis with prominent medullary congestion, and a previous right thyroidectomy with residual left lobe nodular goiter. A small leiomyoma was present at the gastroesophageal junction, and several small gastrointestinal stromal tumors of the stomach wall were seen. Acute and chronic bronchitis was present microscopically, but there was no bronchopneumonia.

**DISCUSSION**

Although more than 20 amyloidogenic precursor proteins have been identified by current molecular methods (5), some forms are more common than others. Furthermore, the subtypes of amyloidosis have markedly different clinical implications. For example, AL amyloidosis, a common systemic form, is due to overproduction of immunoglobulin components associated with immunocyte dyscrasias, and effective treatment may require chemotherapy. AA amyloidosis, in contrast, may be associated with chronic inflammatory disorders, and therapy involves control of the underlying condition. Hereditary-familial forms of amyloidosis may be associated with mutations involving production of an abnormal form of transthyretin (prealbumin), and

![Figure 1. Sagittal section of the heart showing a markedly dilated left atrium with brown endocardial discolorations.](image)

![Figure 2. The left atrium showing heavy amyloid deposits. (a) Congo red stain, ×100.](image)

(b) “Apple-green” birefringence apparent on Congo red stain (polarized), ×100.
management may include genetic counseling and consideration for liver and heart transplantation.

The so-called senile or age-related forms of cardiac amyloidosis can be further divided into two major groups. In one form an otherwise normal or wild type of transthyretin molecule accumulates to form amyloid deposits for generally unknown reasons (6). In so-called IAA, amyloid deposition is limited to the cardiac atria (predominantly the left) as a result of overproduction of atrial natriuretic factor. This subtype of amyloidosis has been cited as one of the most common forms of amyloidosis. The clinical implications of this disorder remain controversial. IAA is frequently associated with atrial fibrillation, but whether this accumulation is its cause is not known. One theory postulates a vicious circle in which atrial dilatation and fibrillation lead to overproduction of atrial natriuretic factor and amyloid deposition, which further exacerbates fibrillation and dilatation (7).

Overall, cardiac amyloidosis remains the primary determinant of prognosis in patients with systemic amyloidosis (3). However, regardless of the subtype of cardiac amyloidosis, this diagnosis may be clinically elusive, and management of these patients may be difficult. The gold standard for diagnosis of cardiac amyloidosis remains endocardial biopsy, but indirect evidence for diagnosis includes echocardiographic evidence of amyloidosis and histologic confirmation of amyloid in non-cardiac tissues.

Diagnostic efforts can be rewarding, as shown by the case above, since a diagnosis of amyloidosis may help explain functional cardiac disturbances and a patient’s failure to respond to therapeutic and supportive measures, even if amyloid is only one contributor to the problem. Furthermore, as previously stated, the clinical implications and management of the various subtypes of amyloidosis are profoundly different; therefore, we encourage molecular subtyping of these disorders whenever possible. Fortunately, such testing is now reasonably available; however, research is still needed in order to improve our understanding of the clinical implications and optimal management of the various forms of cardiac and systemic amyloidosis as we proceed into this era of precision medicine. Furthermore, this case illustrates, once again, the relevance of traditional autopsy, especially when combined with modern and precise molecular tools to elucidate the true nature of a patient’s disease.

Acknowledgment

We thank Jong M. (Jamie) Ko, BA, for photographic and technical assistance.

The Heerfordt-Waldenström syndrome as an initial presentation of sarcoidosis

M. Carter Denny, MD, MPH, and A. Domnica Fotino, MD, MPH

Sarcoidosis is a granulomatous disease of unclear etiology, which commonly presents with cough, dyspnea, chest pain, fever, weight loss, arthralgias, and erythema nodosum. Heerfordt-Waldenström syndrome, a rare presentation of sarcoidosis, is characterized by the presence of parotid gland enlargement, facial palsy, anterior uveitis, and fever. Here we present a case of a 59-year-old nonsmoking African American woman who presented with 3 days of progressively worsening left facial droop, difficulty swallowing, and blurred vision. Over the prior 4 months, she had had a productive cough, fevers, night sweats, and an unintentional 30-pound weight loss. Physical examination revealed a left facial droop involving the forehead, cheek, and chin with an inability to close the left eyelid. Her serum angiotensin-converting enzyme level was twice the upper limit of normal. Prominent hilar markings were identified on chest x-ray, but no focal opacity was seen. Fine-needle aspiration of a preauricular lymph node revealed noncaseating granulomas consistent with granulomatous lymphangitis. The patient was given a diagnosis of Heerfordt-Waldenström syndrome, or uveoparotid fever. Treatment with a high-dose steroid improved her parotid gland enlargement, facial palsy, and anterior uveitis.

CASE REPORT

A 59-year-old nonsmoking African American woman presented with a 3-day history of progressively worsening left facial droop, difficulty swallowing, and blurred vision. Over the prior 4 months, she had had a productive cough, fevers, night sweats, and an unintentional 30-pound weight loss. Physical examination revealed a swollen left cheek and left facial droop involving the forehead, cheek, and chin. She was unable to close her left eyelid completely. Her posterior pharynx was erythematous, but no areas of oropharyngeal fluctuance were noted. Tender, mobile submandibular and cervical lymph nodes were palpable bilaterally, but more prominently on the left. Chest, lung, abdominal, and extremity exams were unremarkable. No rashes were noted. The remainder of the neurologic exam was normal.

Blood cultures, tuberculosis testing, and HIV antibody testing were negative. Antinuclear antibody and extractable nuclear antigen profiles were within normal limits. Serum angiotensin-converting enzyme (ACE) levels were twice the upper limit of normal. Rheumatoid factor was not checked on initial presentation. Computed tomography (CT) of the chest showed hilar lymphadenopathy with bibasilar interstitial lung disease. CT of the neck soft tissues demonstrated enlarged lymph nodes, the largest of which measured 3.2 × 1.2 cm (Figure 1). Esophagogastroduodenoscopy showed pharyngeal edema but no evidence of obstruction. The patient’s ophthalmologic exam was notable for impaired corneal sensation, punctate epithelial erosions in both eyes, and no overt flare or leukocytes seen on slit lamp exam. Fundi were normal in appearance. Fine-needle aspiration of a left preauricular lymph node revealed multinucleated giant cells and noncaseating granulomas consistent with granulomatous lymphangitis (Figure 2). No bacteria or viruses were grown on culture of the biopsied lymph node. The patient was given a diagnosis of Heerfordt-Waldenström syndrome, or uveoparotid fever, which is a rare initial presentation of sarcoidosis.

DISCUSSION

Given the patient’s acute onset of unilateral facial droop, the differential diagnosis includes vascular, infectious, granulomatous, neoplastic, and autoimmune causes of cranial nerve VII injury (Table 1). The principal vascular causes of unilateral facial weakness are ischemic stroke and intraparenchymal hemorrhage involving the cranial nerve VII nucleus. Infectious causes of unilateral facial palsy include herpes simplex virus–associated Bell’s palsy, Lyme disease, HIV, and varicella zoster virus–associated Ramsay-Hunt syndrome. Tuberculosis, orofacial granulomatosis, and sarcoidosis are granulomatous diseases that cause unilateral facial palsy. In tuberculosis, the mastoid, middle ear, or petrous bone is often involved (1, 2). In sarcoidosis, neoplasms such as lymphoma and adenocarcinoma, and autoimmune etiologies such as systemic lupus erythematosus and Sjögren’s disease, the paralysis is thought to be related to inflammation or compression of cranial nerve VII.

Sarcoidosis is a systemic disease characterized by granuloma formation. Typical clinical findings include cough, dyspnea, chest pain, fever, weight loss, arthralgias, and...
syndrome and are caused by a granulomatous inflammatory reaction. The facial nerve palsy is associated with epineural granulomas and perineural inflammatory infiltrates of cranial nerve VII (12). Anterior uveitis classically presents with infected conjunctiva, blurred vision, or eye pain (13). This patient’s blurred vision and eye pain were thought to be related to uveitis. The patient had already received high-dose steroids for 3 days at the time of the full ophthalmologic exam, which may explain why the slit lamp and funduscopic exams were fairly unremarkable. Salivary gland involvement likely led to the pharyngitis seen on esophagogastroduodenoscopy and the patient’s difficulty swallowing.

Table 1. Etiologies of facial nerve palsy

- Ischemic stroke of the pons
- Intraparenchymal hemorrhage of the pons
- Herpes simplex virus–associated Bell’s palsy
- Human immunodeficiency virus
- Lyme disease
- Varicella zoster virus–associated Ramsay-Hunt syndrome
- Sarcoidosis
- Tuberculosis
- Adenocarcinoma
- Lymphoma
- Sjögren’s syndrome
- Systemic lupus erythematosus

only 5% of sarcoidosis cases have neurologic involvement, with the most common manifestation being facial nerve palsy (3–6). Heerfordt-Waldenström syndrome, also called uveoparotid fever, is characterized by the presence of parotid gland enlargement, facial nerve palsy, anterior uveitis, and fever (7–9). Dr. Christian Heerfordt first described this constellation of symptoms in 1909 (10). Dr. Jan Waldenström made the observation that this syndrome was associated with sarcoidosis in 1937 (11). Isolated case reports have described Heerfordt-Waldenström syndrome, but the exact prevalence is not known.

The parotid gland enlargement and cervical lymphadenopathy observed in this patient are typical of Heerfordt-Waldenström syndrome and are caused by a granulomatous inflammatory reaction. The facial nerve palsy is associated with epineural granulomas and perineural inflammatory infiltrates of cranial nerve VII (12). Anterior uveitis classically presents with infected conjunctiva, blurred vision, or eye pain (13). This patient’s blurred vision and eye pain were thought to be related to uveitis. The patient had already received high-dose steroids for 3 days at the time of the full ophthalmologic exam, which may explain why the slit lamp and funduscopic exams were fairly unremarkable.
The diagnosis of Heerfordt-Waldenström syndrome is made by the constellation of symptoms along with an elevated serum ACE level and lymph node biopsy demonstrating noncaseating granulomas. Granulomas in sarcoidosis are known to produce ACE; however, the serum ACE level does not always correlate precisely with disease activity (14, 15). As with other manifestations of sarcoidosis, corticosteroids are the mainstay of treatment. Immunosuppressants such as mycophenolate mofetil, cyclosporine, and infliximab can be utilized in patients whose symptoms are refractory to steroids (16, 17). When complete eye closure is not possible, the patient should use artificial tears while awake, use lubricant eye ointment at night, and cover the affected eye during sleep to prevent exposure keratopathy. If the facial nerve palsy is not treated with steroids, the likelihood of permanent facial paralysis is increased. When the facial paralysis is misdiagnosed as being a simple Bell’s palsy, the opportunity to treat the systemic sarcoidosis is missed. This patient had marked improvement of symptoms after 4 days of prednisone therapy. Two months after discharge, her facial nerve palsy, parotitis, fevers, and uveitis had resolved.

Acknowledgments
We would like to acknowledge Adrian J. Baudy IV, MD, Department of Internal Medicine at Tulane University School of Medicine, for his contributions to the care of this patient.

Unusual dermal pleomorphic calcifications in a case of inflammatory breast carcinoma

Amy R. Yactor, MD, Mehrzad Zarghouni, MD, Jean C. Wang, MD, Raynal R. Hamilton, MD, and Joseph J. Spigel, MD

Inflammatory breast carcinoma is a rare and aggressive type of breast cancer that is definitively diagnosed by histologic evaluation showing invasive tumor cells in the dermal lymphatic system. Associated dermal calcifications are not typically identified. We report an unusual case in which inflammatory breast carcinoma led to the presence of pleomorphic dermal calcifications identified on the initial mammographic examination.

CASE REPORT

A 52-year-old woman presented for her yearly left breast diagnostic mammogram with recently developed erythema of the left breast. She had a history of right mastectomy for invasive ductal carcinoma and multifocal ductal carcinoma in situ (DCIS) in 2005 and left breast lumpectomy for focal DCIS in 1993.

Routine and magnification mammogram views of the left breast revealed interval development of increased density in the upper inner quadrant with associated pleomorphic calcifications in a segmental distribution, skin thickening, as well as dermal pleomorphic calcifications (Figure 1). Subsequent skin punch biopsy yielded infiltrating ductal carcinoma with dermal lymphatic invasion and coarse dermal calcifications (Figure 2). Physical and mammographic examination findings of dermal thickening and erythema consistent with inflammatory breast cancer corresponded to the pathologic diagnosis of dermal lymphatic invasion.

DISCUSSION

Inflammatory breast cancer is a rare and aggressive type of breast cancer making up less than 5% of all breast cancer cases. It is characterized by rapid progression, local and distant metastases, young age of onset, and lower overall survival compared with other breast cancers (1). It is suspected clinically when there is skin thickening, edema, and erythema and is often initially misdiagnosed as a benign infectious process. The diagnosis is confirmed by biopsy with histologic analysis showing invasive tumor cells in the dermal lymphatics; however, the dermal layer does not typically have associated calcifications. We present this case as an example of inflammatory breast cancer with associated dermal calcifications identified on mammography definitively diagnosed by skin punch biopsy. To the best of our knowledge, a similar case has not been reported.

Fine pleomorphic calcifications are well known for being associated with malignancy in the breast parenchyma, most notable for the association with DCIS, particularly when identified in a segmental, branching, or linear pattern (2). It is very rare, however, to have similar appearing pleomorphic calcifications within the affected lymphatic system and further distant metastatic sites. A few reported cases have been described of metastatic axillary lymph nodes containing pleomorphic calcifications. The two cases reported by Walsh et al found that one patient had similar appearing calcifications in the ipsilateral breast, and another patient had an asymmetric density without associated calcifications in the ipsilateral breast parenchyma (3). In another series of 50 patients with metastatic axillary disease, 3% had intranodal calcifications identified mammographically (4). The presence of similar appearing pleomorphic dermal calcifications in inflammatory breast carcinoma has not yet been reported.

It is rare to have dermal calcifications that are associated with malignancy. When calcifications are located in the dermal layer, they are typically thought to be benign, and if confirmed to be dermal in location on tangential mammogram views, no additional workup is needed (5). The American College of Radiology BI-RADS lexicon describes mammographic findings using a standard nomenclature, and benign calcifications include those that are located in the skin (6). Typical skin calcifications are usually related to a chronic inflammatory process such as folliculitis and are most often located in sebaceous glands in the dermal layer. These most often appear as small, well-demarcated calcifications with lucent centers rather than as pleomorphic calcifications, as seen in this patient (7).
Acknowledgments

The authors thank William G. Herlihy, MD, in the Department of Pathology at Baylor University Medical Center at Dallas for providing the histopathologic images.


Figure 1. (a) Routine left lateromedial oblique and (b) left craniocaudal diagnostic mammogram images show an area of increased density with associated pleomorphic calcifications in a segmental distribution in the upper inner breast (blue arrows) and skin thickening with pleomorphic dermal calcifications (white arrows). Thin radiopaque markers indicate the sites of scars from previous surgery. (c) Magnification 90-degree lateromedial and (d) magnification craniocaudal views better demonstrate the increased density and pleomorphic calcifications in the upper inner left breast (blue arrows) and associated skin thickening with dermal microcalcifications (white arrows).

Figure 2. Photomicrographs of the specimen from the skin punch biopsy on (a) low power and (b) medium power show infiltrating ductal carcinoma in the dermal layer (black arrows) and coarse fragmented microcalcifications in the dermal layer (blue arrows). (c) Photomicrograph of the specimen from a different site in the deep dermis on high power shows coarse fragmented calcifications (blue arrows) with an adjacent focus of invasive ductal carcinoma (black arrow).
Get a mammogram
Like your life depends on it.

14th Annual Celebrating Women Luncheon
When: October 23, 2013
Where: Hilton Anatole Hotel, Dallas
Call 1.800.4BAYLOR
www.baylorhealth.com/celebratingwomen
Salivary gland-like neoplasms of the breast are a known entity. A single novel case of basal cell adenoma of the breast is presented, and the presentation, treatment, and morphologic features of this case are discussed.

Although still relatively uncommon, in recent years salivary gland-like neoplasms of the breast have become increasingly recognized as an entity. In a 2003 review of salivary gland-like tumors of the breast, several lesions were described, including pleomorphic adenoma, adenoid cystic carcinoma, benign and malignant myoepitheliomas, syringomatous carcinoma, adenomyoepithelioma, acinic cell carcinoma, oncocytic carcinoma, and mucoepidermoid carcinoma (1). Subsequently, a case series of basal cell adenocarcinoma of the breast was presented (2). However, basal cell adenoma of the breast appears to be exceedingly rare with no cases reported in recent reviews (1, 3, 4). Here we present a case of basal cell adenoma of the breast along with its histologic and immunohistochemical profile.

CASE REPORT

A 90-year-old white woman with prior mitral valve prolapse repaired in 2004 and hypothyroidism presented with a 3-year history of an enlarging left nipple. No biopsies or imaging had been performed. On examination, the left nipple was larger than the right one, and the skin over it had a slightly purplish discoloration compared to the right. There was no nipple discharge and no enlargement of the axillary or supraclavicular lymph nodes.

A mammogram was essentially negative, and a sonogram of the left breast showed a separate subcentimeter hypoechoic density in the 11:00 position located approximately 1 cm from the nipple, adjacent to the larger clinically apparent mass. Both lesions were excised. Histologically, the larger lesion within the left nipple was relatively well circumscribed and composed of a lobulated proliferation of epithelial elements. There was prominent palisading of cells at the periphery of the epithelial nests, giving the lesion a “basaloid” appearance (Figure). Additionally, there were focal areas showing slightly more proliferation with cytologic monotony and mildly increased mitotic activity. No features of malignancy were present. Immunohistochemically, most cells stained positive for p63, and smooth muscle actin highlighted the myoepithelial cells within the lesion. Overall, the histologic and immunohistochemical profile most closely resembled a basal cell adenoma. The separate lesion located at the 11:00 position 1 cm from the nipple was characterized by mostly benign breast tissue with apocrine metaplasia, apocrine cysts, and focal ectatic ducts.

DISCUSSION

Salivary gland-like neoplasms of the breast are well documented (1). Most are pleomorphic adenomas with only infrequent examples of other salivary gland-like neoplasms (1). From an embryological standpoint, the occurrence of salivary gland-like neoplasms in the breast should not be too surprising considering the breast and salivary glands are both modified sweat glands. Both are tubuloacinar glands, which share many histologic features. Therefore, overlapping pathologic features is not an unreasonable expectation. Basal cell adenomas are classically associated with the salivary glands. First described by Kleinhasser and Klein in 1967 (5), they were formally included in the World Health Organization classification in 1991 (6). According to the Armed Forces Institute of Pathology registry, basal cell adenomas are rare, accounting for about 2% of all benign salivary gland tumors (7). Most of these lesions occur in the major salivary glands (75% parotid and 5% submaxillary gland) in adults. There is a 2:1 female predilection. Grossly, these lesions are fairly well circumscribed and solitary and can be treated with conservative excision with a low recurrence rate.

Histologically, there are five morphologic variants of basal cell adenoma. The solid type is the most common, followed by the trabecular and trabecular-tubular types. The membranous and pure tubular variants are the least common. All variants lack a myxochondroid matrix, as seen in pleomorphic adenomas, and have a fibrous stroma. The most common pattern of proliferation is that of cytologically bland basaloid cells with peripheral palisading seen within the cellular nests. All variants can...
Basal cell adenoma of the breast demonstrate cystic change, keratinization, and squamous whorls (8). Although morphologically inapparent, there is myoepithelial differentiation in all variants of basal cell adenoma. These myoepithelial cells can be demonstrated by immunohistochemical stains for smooth muscle proteins.

The main differential diagnosis of basal cell adenoma includes basal cell adenocarcinoma. Findings can be subtle between the two entities; therefore, it is important to distinguish between them. Basal cell adenocarcinoma differs from basal cell adenoma by virtue of its infiltrative spread, perineural and lymphovascular invasion, and variable degree of cytologic atypia and mitotic activity. Additionally, immunohistochemical stains can help in differentiating these two entities. Basal cell adenocarcinomas have been known to express p53, BCL2, and epidermal growth factor receptor (9). In the present case, the lesion was well circumscribed and encapsulated with no evidence of an infiltrative pattern of growth. No perineural or vascular invasion was identified. The cells were monotonous with minimal cytologic atypia and focal areas of mildly increased mitotic activity. Overall, these features best fit with a basal cell adenoma.

Figure. Morphology of basal cell adenoma of the breast. (a) Low-magnification picture showing the relationship to the overlying skin. Note the well-circumscribed edge of the lesion with the underlying dermis (hematoxylin and eosin, ×40). (b) Medium magnification emphasizing the trabecular architecture with fibrotic stroma (hematoxylin and eosin, ×200). (c) High magnification of the lesion showing cellular nests of monotonous cells with minimal cytologic atypia. Note the peripheral palisading (hematoxylin and eosin, ×400). (d) Immunohistochemical stain for p63, a nuclear stain, showing positive staining in many of the tumor nuclei (×400).

Critical lower limb ischemia from an embolized Angio-Seal closure device

Chris Cianci, DO, Robert C. Kowal, MD, PhD, Georges Feghali, MD, PhD, Stephen Hohmann, MD, Robert C. Stoler, MD, and James W. Choi, MD

Vascular closure devices were introduced in the early 1990s in an effort to reduce time to hemostasis, enable early ambulation, and improve the comfort of patients undergoing femoral artery access for endovascular procedures. Many of these devices leave a foreign component in or around the artery, which can lead to complications such as hematoma, pseudoaneurysm, infection, or limb ischemia. Here we present a case where device embolization led to arterial occlusion and critical limb ischemia.

CASE REPORT

A 51-year-old woman with ventricular premature complex-induced cardiomyopathy was referred to Baylor University Medical Center at Dallas for an electrophysiology study and possible radiofrequency ablation. Her right common femoral artery was accessed for the procedure, and the electrophysiology study and radiofrequency ablation were performed without incident.

An Angio-Seal (St. Jude Medical, St. Paul, MN) was employed to close the femoral artery puncture site. The Angio-Seal device consists of three bioabsorbable components to actively seal the arteriotomy. The anchor is placed against the inside of the arterial wall. The collagen plug sits on top of the arteriotomy in the tissue tract. The suture and compaction tube cinch the anchor and collagen together to form a secure seal (Figure 1). In this patient, as the compaction tube was advanced, the suture snapped near the sheath. The compaction tube was removed and the suture cut near the skin surface. This resulted in partial hemostasis with some continued oozing but no pulsatile flow or hematoma. Complete hemostasis was obtained with manual compression. The patient was observed overnight and discharged the next morning without incident.

Several days later she began to experience right leg claudication after walking 100 feet. On examination, she had a cool right lower extremity with diminished peripheral pulses. Examination of the left lower extremity was normal. A computed tomography scan was performed at an outside hospital and revealed critical right tibioperoneal trunk stenosis. Intravenous heparin therapy was initiated, and she was transferred to Baylor University Medical Center at Dallas.

She underwent an aortobifemoral angiogram performed via a 5 French left common femoral micropuncture. Digital subtrac-

tion angiography of both limbs demonstrated a large amount of thrombus in the distal right popliteal artery extending into the tibioperoneal trunk. The anterior tibial artery was occluded at the ostium. There was a 99% stenosis at the tibioperoneal trunk (Figure 2). Manual and rheolytic thrombectomy were performed, and a 4 French Cragg-McNamara infusion catheter was placed in the distal right popliteal artery for alteplase thrombolysis. After 36 hours of intermittent thrombolysis, a large thrombus burden remained and operative embolectomy was performed in the distal popliteal and proximal tibial arteries. In addition, the remnants of the Angio-Seal closure device (string and collagen plug) were removed from the distal popliteal artery. She tolerated the procedure well and peripheral pulses returned to normal. She was discharged 2 days later.

DISCUSSION

For several decades, manual compression followed by hours of bedrest was the sole method of femoral artery puncture site
hemostasis. Compression requires a trained medical professional to maintain pressure on the access site for up to 30 minutes, depending on sheath size, anticoagulation status, and several other patient and procedural characteristics. While this method is highly effective, it can also be extremely uncomfortable for the patient and labor intensive for the medical staff.

In the early 1990s vascular closure devices (VCDs) were introduced as an alternative to manual compression, and today a variety of VCDs are available. The appeal of early ambulation and enhanced patient comfort, as well as the reduction of cost associated with manual compression and in-hospital observation, has made the use of VCDs commonplace. It is estimated that over 1 million VCDs are used yearly in the United States (1).

Complications related to VCDs may be broadly classified into three categories: hemorrhagic, obstructive, and infective (10). The most feared complication of VCDs is limb ischemia. This can occur as a result of embolization, thrombosis, or occlusion from the intravascular component of the device (11). Several studies have reported the incidence of lower limb ischemic complications following Angio-Seal use (12–16). Thalhammer et al reported their single-center experience with Angio-Seal–related ischemic complications. They noted 14 instances of symptomatic lower limb ischemia in 7376 patients (0.2%) undergoing catheterization between 2003 and 2006 (12). Castelli et al discovered 4 cases of lower limb ischemia in 175 patients who received an Angio-Seal following cardiac catheterization (2.3%) (13). One possible explanation for the wide variation in ischemic complication rates may be operator experience. Balzer et al clearly demonstrated that VCD delivery success rates increased as the operator’s experience and familiarity with the device increased (17).

Limb ischemic symptoms can present acutely in the minutes after device deployment, but may also have a subacute presentation with claudication in the days or weeks following the procedure (18). Endovascular approaches to treat limb ischemia caused by VCDs have been described, but most authors recommend direct surgical cutdown, retrieval of the device, and definitive arterial repair, most often with venous patch plasty (10). Steinkamp et al reported on their experience using excimer laser and balloon angioplasty in 13 patients with lower limb ischemic symptoms as a result of either vessel occlusion or stenosis related to an Angio-Seal device. Four of the 13 patients had complete vessel occlusion while the remaining 9 had lower-extremity vessel stenosis. All patients were successfully treated and experienced increased walking distance and an improved ankle-brachial index immediately following the procedure and at 3- and 6-month follow-up (19).

Although endovascular or open surgical treatment of limb ischemia resulting from VCDs can be limb sparing, it can be associated with additional significant morbidity. Wille et al described several cases of limb ischemia resulting from Angio-Seal deployment (18). One patient required a four-compartment fasciotomy of the lower leg to treat reperfusion-induced compartment syndrome. In addition, the lateral skin defect needed split skin grafting 6 weeks after the procedure. A second patient experienced postoperative groin infection that required debridement, sartorius muscle transposition, and a prolonged course of intravenous antibiotics. Fortunately, our patient had no postoperative sequelae.

While VCDs may reduce the time to ambulation and discharge, enhance patient comfort, improve staff efficiency, and received manual compression. The risk of experiencing any vascular complication was 1.1% in the VCD group and 1.7% in the manual compression group ($P < 0.001$) (9). In 2004, Nikolsky et al conducted a metaanalysis of 30 studies involving 37,066 patients undergoing cardiac catheterization. In this study vascular complication rates were higher in the patients who received a VCD (odds ratio 1.34; 95% confidence interval 1.01–1.79) (6).

Figure 2. Angiogram showing thrombus in the right popliteal artery with an occluded anterior tibial artery.
reduce costly in-hospital monitoring, they can expose patients to additional risks, which can be life and limb threatening. Physicians, nurses, and ancillary staff must be aware of such risks, recognize early signs of potential problems, and act expeditiously.

The myth of the Bernheim syndrome

Monica S. Chung, BS, Jo Mi Ko, BA, Themistokles Chamogeorgakis, MD, Shelley A. Hall, MD, and William C. Roberts, MD

The Bernheim syndrome has been a topic of discussion for over a century. It has been reported to be caused by severe rightward movement of the ventricular septum resulting in compression of the right ventricular cavity leading to right-sided heart failure without pulmonary congestion. Hemodynamic findings have been described in a few patients with the so-called Bernheim syndrome. We describe a patient in whom the ventricular septum dramatically decreased the size of the right ventricular cavity and yet peak systolic pressures in both the right ventricle and pulmonary trunk were identical. Thus, it is difficult to view the Bernheim syndrome as a real entity.

In 1910, Hippolyte Bernheim (1840–1919) (Figure 1) described 10 patients with signs and symptoms of right-sided heart failure, and necropsy in each disclosed a thick left ventricular free wall and ventricular septum with the latter bulging into the right ventricular cavity (1). He titled this original article “Venous asystole in hypertrophy of the left heart with associated stenosis of the right ventricle.” In that article Bernheim included two drawings, one of a normal heart and one with a thickened left ventricular wall with the thick ventricular septum protruding toward the right ventricular cavity (Figure 2). In 1915, Bernheim published a similar article (2), this time titling it “Right ventricular stenosis caused by displacement of the septum in eccentric hypertrophy of the left ventricle and resulting venous asystole.”

During the next century, a number of articles appeared describing “the Bernheim syndrome.” Although Bernheim described 10 cases in his original article, most subsequent articles have been only case reports (3–11), with few exceptions (1, 12–22). Most subsequent articles were necropsy studies, and most supported the concept of the Bernheim syndrome's being a real entity. There were exceptions. Evans and White (12) (Figure 1) studied 33 patients at necropsy with considerable left ventricular hypertrophy (heart weight >750 g) and then reviewed their medical records to determine whether signs and symptoms of right-sided heart failure were isolated or simply preceded signs of left-sided heart failure (dyspnea). These authors found no instance . . . of isolated early signs or symptoms of right-sided failure . . . [and] concluded from . . . [their] analysis, as well as from prior experience, that . . . [they had] yet to encounter any unquestionable case of so-called Bernheim's syndrome . . . [and that] it would appear sensible to drop this designation.

In 1955, Selzer and colleagues (6) (Figure 1) described a 62-year-old man with severe hypertension (blood pressure 260/140 mm Hg) hospitalized because of nausea, hepatomegaly, distended neck veins, and clear lung fields. Right-sided cardiac catheterization disclosed identical peak systolic pulmonary arterial and right-ventricular pressures (87 mm Hg) and identical right atrial mean and right ventricular end-diastolic pressures (18 mm Hg). A few days later, the patient died rather suddenly. His heart weighed 690 g. A cross-section of the cardiac ventricles in this patient is shown in Figure 3. Selzer et al argued rightfully that “‘encroachment’ of the cardiac septum on the cavity of the right ventricle appears to be a normal phenomenon, or may be an accentuation of normal conditions by left ventricular hypertrophy.” The authors further argued “that the theoretic criteria for the pathologic diagnosis of the Bernheim syndrome have not been fulfilled by the majority of cases [reported].” These authors concluded by stating “that the necropsy findings alleged to ‘prove’ the existence of Bernheim’s syndrome are based on misconceptions of the normal relationship and are therefore unacceptable. . . . [The authors] hoped that the term [the Bernheim syndrome] eventually will be dropped from current terminology.” Surprisingly, Selzer and associates did not emphasize or even mention the lack of right ventricular inflow or outflow obstruction documented hemodynamically in their patient.

Despite the convincing arguments against the concept of the Bernheim syndrome by Evans and White and by Selzer...
and colleagues, cases purported to represent this syndrome continued to be published during the next decades, including its mention in a recent prominent cardiologic text (23). Described herein is a patient in whom the ventricular septum from apex to base nearly obliterated the right ventricular cavity and yet cardiac catheterization 40 days before cardiac transplantation had shown identical pulmonary arterial and right ventricular peak systolic pressures.

CASE STUDY

A 71-year-old hypertensive retired college professor apparently had been well until age 48 years when he had a large myocardial infarct, and at age 54, probably a second myocardial infarct followed shortly by percutaneous coronary intervention with stents inserted in both right and left anterior descending coronary arteries. During subsequent years he developed evidence of severe heart failure, runs of ventricular tachycardia, atrial fibrillation, and a murmur consistent with mitral regurgitation. An intracardiac defibrillator was inserted when he was 63 years old. The left ventricular ejection fraction on some occasions was as low as 10%.

When seen at Baylor University Medical Center at Dallas initially in December 2012, he had evidence of severe pulmonary congestion, which rapidly resolved with anti–heart failure drugs. His lungs then were normal to auscultation and by radiography. In April 2013, a right-sided cardiac catheterization was performed (Figure 4). The pulmonary arterial mean wedge pressure was 12 mm Hg. His body mass index was 24 kg/m². Just prior to cardiac transplantation (performed in May 2013), he was on 18 medications.

The explanted heart, which weighed 505 g, had extensive left ventricular and ventricular
septal scarring with enormous dilatation of the left ventricular cavity and compression of the right ventricular cavity by the ventricular septum (Figures 5 and 6).

COMMENTS
After review of previous articles, including photographs of the heart (3, 6–8, 13, 15–18), none actually showed in our view compression of the right ventricular cavity by the ventricular septum. In our patient, however, there was marked left ventricular dilatation with clear compression of the right ventricular cavity. Peak systolic pressures in both the right ventricle and pulmonary trunk, however, were identical, indicating the absence of “right ventricular stenosis” despite the appearance thereof from examination of the explanted heart. Thus, we agree with Evans and White.

Figure 4. Hemodynamic tracings from cardiac catheterization in our patient: (a) right atrium; (b) pulmonary artery; (c) right ventricle, and (d) pulmonary capillary wedge pressure, all in mm Hg.

Figure 5. Explanted basal portion of the heart of our patient. The arrow shows a slit-like right ventricular (RV) cavity. The left ventricular (LV) cavity is severely dilated, and its wall is focally scarred. The ventricular septum (VS) protrudes severely toward the right ventricular cavity.

Figure 6. Explanted 1-cm thick slices of the ventricles caudal to the basal portion of the heart in our patient. The arrows show the extremely small right ventricular (RV) cavity. LV indicates left ventricle; VS, ventricular septum.
and with Selzer et al that “the Bernheim syndrome” is a nonentity and should be dropped from our medical lexicon.

Fibromuscular dysplasia is an uncommon cause of secondary hypertension. When the resulting hypertension cannot be successfully treated with medications, balloon angioplasty has been shown to be successful by disrupting the “webs” of tissue in the renal artery. We present a case of secondary hypertension due to fibromuscular dysplasia and the successful treatment with balloon angioplasty.

CASE DESCRIPTION
A 61-year-old woman was referred to Baylor University Medical Center at Dallas for severe hypertension, uncontrolled on several medications. Approximately 1 year earlier, she had been evaluated for “food poisoning” and headache. At that time she was found to have a systolic blood pressure of 180 mm Hg. She subsequently developed a left parietal bleed. She was treated with carvedilol and hydrochlorothiazide, but because of her age, the sudden onset, and the severity of the hypertension, secondary causes were suspected. A meta-iodobenzylguanidine test was performed. It was believed to be positive, and a left adrenalectomy was performed. Despite medical therapy and the adrenal gland resection, she continued to have severe hypertension, with blood pressures in excess of 180 mm Hg systolic at home. A magnetic resonance angiogram (MRA) of her renal arteries showed “beads on a string” in her right renal artery. As this was suggestive of fibromuscular dysplasia (FMD), she was referred for invasive renal artery angiography. The angiogram demonstrated FMD and balloon angioplasty was successfully performed (Figure). On follow-up clinic visits, her blood pressure had normalized on only a low dose of angiotensin-converting enzyme inhibitor.

DISCUSSION
FMD is a disease of unknown etiology that results in “webs” of tissue which perturb the flow of blood through arterial vasculature. It commonly involves the renal and carotid arteries, although it can involve vertebral, iliac, subclavian, and visceral arteries. Disease manifestation may vary widely depending on the arterial segment involved and its severity (1). In adults, women account for about 90% of the cases.

Renal FMD accounts for about 70% of this disease process. In adults it accounts for about 10% of renovascular hypertension. FMD of the renal arteries is bilateral in about 40% of patients (2). Clinical manifestations are usually a consequence of decreased flow across the renal webs.

Severe resistant hypertension, a sudden rise in blood pressure, and increased serum creatinine upon initiation of angiotensin-converting enzyme inhibitors are common presentations of FMD and should be included in the differential diagnosis when young women present with accelerated hypertension, especially if there is intolerance to antihypertensive medication. Abdominal bruits can sometimes be heard.

Angiography is the gold standard for the diagnosis of FMD, but the diagnosis can be made by noninvasive tests (3). Computed tomographic angiography is good at detecting FMD. Duplex ultrasound is highly operator and center dependent, but can suggest the diagnosis. MRA has a sensitivity of about 20% and is not as diagnostic for FMD. “Beading” is an important and common angiographic finding and is present in >90% of cases.

Treatment options include both medical therapy and revascularization. Conservative treatment involves adequate control of blood pressure with antihypertensive drugs, but stenosis may lead to renal dysfunction and loss of renal parenchyma. Other limitations of medical therapy include the need for frequent monitoring of blood pressure and renal function.

Revascularization can cure hypertension in more than half of the cases and can lower the blood pressure in another 25% of the cases. Percutaneous balloon angioplasty has become the preferred method of revascularization with a low complication rate and good results (4, 5). Stents are typically used only as a bailout (i.e., if there is dissection or disruption of the renal artery), but are not typically necessary to achieve a hemodynamically satisfactory result.

From the Divisions of Cardiology (Hundae, Schussler) and Nephrology (Hebert), Department of Internal Medicine, Baylor University Medical Center at Dallas; and the Texas A&M Health Science Center, College of Medicine (Hebert, Schussler).

Corresponding author: Jeffrey M. Schussler, MD, 621 North Hall Street, Suite 500, Dallas, TX 75226 (e-mail: Jeffrey.Schussler@BaylorHealth.edu)

Figure. (a) Right renal artery demonstrating fibromuscular dysplasia (FMD) and a classic “stacked coins” or “beads on a string” appearance (arrow). (b) An angioplasty balloon (5 x 20 mm) was inflated in the area of FMD (arrow). (c) With successful result (arrow). Note that while there is reduction of the visible “webs” of tissue, the final result does not demonstrate complete resolution of the angiographic appearance of the FMD.
A 63-year-old man came to the emergency department because he was lightheaded and dyspneic and felt “skipped heart beats.” An electrocardiogram showed sinus P waves at a rate of 44 per minute and repeated sequences of a right ventricular escape complex that occurred nearly simultaneously with one of the sinus P waves, a conducted normal QRS complex with a P-R interval of 0.19 seconds, and a ventricular premature complex with a retrograde P wave that reset the sinus node (Figure).

The problem was the slow sinus rate. It allowed the right ventricular pacemaker to escape and, by causing temporal dispersion of repolarization after the conducted QRSs, facilitated reentrant ventricular premature complexes with retrograde atrial conduction that reset the sinus node, thus slowing it further. There are many causes of sinus bradycardia. Among them are medications. This hypertensive man was taking clonidine 0.3 mg twice a day and diltiazem 90 mg twice a day, both orally. The combination of two or more drugs that can slow the sinus node, such as beta-adrenergic blocking drugs, non-dihydropyridine calcium-channel blockers, and clonidine, has on occasion caused profound sinus bradycardia (1, 2) and may also result in significant atrioventricular nodal block (3).

A 53-year-old woman first had a heart murmur noted at age 3. She was symptom free until age 47 but since then has had repeated episodes of cardiac failure. On this occasion she noted increasing shortness of breath, bilateral leg edema up to her knees, and a 10-lb weight gain over a week's time. Increasing her furosemide from 20 to 40 mg daily did not relieve her symptoms.

On physical examination, this small, slender woman had a blood pressure of 140/84 mm Hg, bilateral expiratory wheezes, and crackles at both lung bases. Neck veins were elevated to 15 cm above the angle of Louis, and there was 1–2+/4+ edema up to her knees. A 2+/4+ right ventricular lift was felt at the left sternal edge. A hyperdynamic 4+/4+ left ventricular impulse was felt and a third heart sound was heard in the anterior axillary line. A 4+/6+ continuous murmur peaked at the second heart sound and was best heard in the second left intercostal space. There are many causes of continuous murmurs. When the intensity of the murmur peaks at the second heart sound and the murmur is loudest in the second left intercostal space or just below the medial portion of the left clavicle, the cause is almost always a patent ductus arteriosus. When the murmur is maximal elsewhere, the cause usually is not a ductus.

An electrocardiogram (Figure) recorded at half standard, i.e., 1 mV = 5 mm, showed sinus rhythm with atrial premature complexes, biatrial enlargement, left axis deviation of the QRS

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

Corresponding author: D. Luke Glancy, MD, 7300 Lakeshore Drive, #30, New Orleans, LA 70124 (e-mail: dglanc@lsuhsc.edu).
complex (−35°), and left ventricular hypertrophy with repolarization abnormality, including a long QT interval (405 ms with a QTc of 473 ms). Although left ventricular hypertrophy with repolarization abnormality, i.e., a wide angle between the QRS and the ST-T vectors, is classically seen with pressure overload of the left ventricle, such as occurs with systemic hypertension or aortic stenosis, this repolarization change may occur whenever left ventricular hypertrophy is severe, no matter the cause (1).

The chest radiograph demonstrated a huge cardiac silhouette, prominent pulmonary vasculature, bilateral pulmonary edema, and scoliosis of the spine, which is more common in patients with congenital heart disease than in the general population.

In the past, patients with patent ductus arteriosus occasionally have lived to be far older than our patient (2), but for 75 years now closure of the arterial duct, first by surgical ligation (3) and more recently by catheter-delivered closure devices (4), has been available as a highly effective and relatively low-risk cure for the malformation. Consequently most arterial ducts are now closed in infancy or early childhood. Our patient, however, has always refused any invasive treatment. In her, the duct is large enough to allow a moderately large left-to-right shunt that over time has produced severe left atrial and left ventricular enlargement. Although her left ventricular ejection fraction 18 months ago was 50% as judged by echocardiogram, the left ventricle clearly is failing and the resulting pulmonary arterial hypertension has caused right ventricular and right atrial enlargement. This has been accentuated by chronic obstructive pulmonary disease caused by her smoking 1½ packs of cigarettes per day for 25 years and manifested by a forced expiratory volume in 1 second of 35% and wheezing even when she is not in overt cardiac failure, and by a hemoglobin of 17 g/dL and a hematocrit of 53% on the current admission.

The patient responded to medical treatment for congestive heart failure but was lost to follow-up after discharge.

We describe the case of a 24-year-old woman who intentionally ingested between 400 and 600 mg of amlodipine along with a large number of simvastatin and trazodone tablets.

**CASE HISTORY**

A 24-year-old white woman with a past history of depression being treated with sertraline presented to the emergency department with nausea, vomiting, and diarrhea after ingesting 400 to 600 mg of amlodipine and unknown quantities of simvastatin and trazodone. The quantities ingested were deduced based on the last refill date and contacting the pharmacy. The patient had one previous suicide attempt while in high school. She reported a recent altercation with her estranged husband and a history of alcohol abuse and rehabilitation. She was sober until the night of the overdose, when she had a beer. She smoked 30 cigarettes each day and denied the use of any illicit drugs.

In the emergency department, she was euthermic with a heart rate of 99 beats/minute, in no distress, but with a blood pressure of 72/34 mm Hg. Her skin was cold and clammy. Her laboratory results at presentation are shown in Table 1.

She received 3 L of normal saline and 1 L of 5% dextrose in normal saline in the emergency department. Because the hypotension remained refractory, vasopressor agents were initiated with dopamine and norepinephrine followed by vasopressin and phenylephrine. The patient was intubated for airway protection. Glucagon was started with a 10 mg bolus followed by a continuous infusion at 10 mg/h. A 20% fat emulsion (Intralipid) was started with a 1.5 mg/kg bolus over 10 minutes followed by 0.25 mL/kg/h. A calcium gluconate drip was started at a rate of 1 g/h. In addition, an intravenous insulin infusion was started at a rate of 70 units/h along with 10% dextrose. The patient started developing metabolic acidosis in spite of an intravenous isotonic bicarbonate infusion. Continuous venovenous hemodialysis without any ultrafiltration was started for the worsening metabolic acidosis and the anuria. Intravenous hydrocortisone was administered at a dose of 50 mg every 8 hours.

On the second day of hospitalization, a chest radiograph showed worsening bilateral pulmonary infiltrates. With numerous catecholamines, the heart rate was up to 140 beats per minute and the respiratory rate increased to 35 breaths per minute. A fractional inspired oxygen concentration (FiO₂) at 100% was instituted. Ultrafiltration was started with continuous venovenous hemodialysis. Dopamine and lipid emulsion infusions were discontinued as hemodynamic stability improved.

By the third hospital day, the patient’s heart rate had slowed, but leukocytosis developed. Meropenem and levofloxacin were added. Phenylephrine was tapered, and albumin 25 g every 8 hours was started to aid in vasopressor tapering.

By the fourth day of hospitalization, the FiO₂ was reduced to 60% with maintenance of good oxygen saturation. A chest radiograph showed improvement in the pulmonary infiltrates. The high-dose insulin drip was discontinued and the calcium gluconate drip was decreased to 0.5 g/hour. Vancomycin was started for methicillin-resistant *Staphylococcus aureus* coverage and the intravenous bicarbonate was stopped. The following day, vasopressin and norepinephrine were tapered off.

Two days later, glucagon and calcium gluconate were discontinued. The patient was extubated on the ninth day of admission and transitioned to intermittent hemodialysis. The patient’s continued kidney failure was attributed to acute tubular necrosis from hypotension and rhabdomyolysis. The rhabdomyolysis reached a peak creatine phosphokinase of 5035 U/L 50 hours after ingestion. This eventually resolved without the need for continued hemodialysis 17 days after continuous venovenous hemodialysis was first initiated. Her creatinine at the time of discharge was 1.7 mg/dL. She was discharged home 23 days after admission.

**DISCUSSION**

Amlodipine, a dihydropyridine calcium channel blocker, has a half-life of approximately 30 to 50 hours and a large volume of distribution (2 L/g). Its slower and longer (up to 72 hours) duration of action, relative lack of negative inotropy, and once-daily dosing has made it preferred over other calcium channel blockers (CCBs) such as verapamil or nifedipine. CCBs such as amlodipine reduce calcium flux through voltage-gated slow
The major toxic effect of an overdose is refractory hypotension, due to both vasodilation and impaired cardiac metabolism and contractility. Tissue ischemia and lactic acidosis ensue. Blockade of calcium channels in other tissues, such as pancreatic beta cells, also has other important adverse consequences (i.e., reduced insulin release).

Intravenous volume expansion (using sodium bicarbonate–containing solutions to simultaneously attempt to correct the lactic acidosis) and multiple vasopressors are routinely initiated, but this treatment is often ineffective (1) because the primary mechanism of hypotension is arterial muscle relaxation and not hypovolemia. Calcium infusion provides a direct antidote and may be helpful; however, the response to calcium is also often inadequate (2). Given its relatively benign intervention, even in the presence of high serum concentrations acutely, calcium is still often utilized in these patients. Glucagon may be infused because it activates myocardial adenylate cyclase and thus increases cardiac cyclic adenosine monophosphate levels, which results in an inotropic effect. High-dose insulin infusion together with adequate glucose to maintain normal glucose levels—so-called “hyperinsulinemia/euglycemia therapy”—has been shown to be very effective in experimental models of CCB overdose (3, 4). Insulin has a direct positive cardiac inotropic action and may also improve myocardial carbohydrate oxidation, which is often impaired in these patients. Finally, intravenous lipid infusions have recently been used to treat lipid-soluble drug overdoses (5–8). Raising serum lipid levels can markedly increase the drug’s volume of distribution and thereby reduce its effective plasma level. Furthermore, provision of triglycerides provides an alternative energy source for the myocardium.


Table 1. Laboratory results obtained during the patient's early hospitalization for amlodipine overdose

<table>
<thead>
<tr>
<th>Test</th>
<th>Admit</th>
<th>12 h</th>
<th>24 h</th>
<th>36 h</th>
<th>50 h</th>
<th>80 h</th>
<th>110 h</th>
<th>140 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (mEq/L)</td>
<td>140</td>
<td>139</td>
<td>141</td>
<td>138</td>
<td>140</td>
<td>137</td>
<td>135</td>
<td>138</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>4.2</td>
<td>4.1</td>
<td>3.6</td>
<td>3.4</td>
<td>3.9</td>
<td>4.3</td>
<td>5.5</td>
<td>4.5</td>
</tr>
<tr>
<td>Chloride (mEq/L)</td>
<td>107</td>
<td>113</td>
<td>111</td>
<td>104</td>
<td>107</td>
<td>105</td>
<td>102</td>
<td>103</td>
</tr>
<tr>
<td>Carbon dioxide (mEq/L)</td>
<td>17</td>
<td>13</td>
<td>17</td>
<td>25</td>
<td>23</td>
<td>21</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dL)</td>
<td>15</td>
<td>17</td>
<td>18</td>
<td>9</td>
<td>5</td>
<td>3</td>
<td>14</td>
<td>20</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>2.6</td>
<td>2.7</td>
<td>2.2</td>
<td>1.1</td>
<td>1.3</td>
<td>1.1</td>
<td>1.2</td>
<td>1</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>150</td>
<td>148</td>
<td>328</td>
<td>135</td>
<td>103</td>
<td>292</td>
<td>160</td>
<td>147</td>
</tr>
<tr>
<td>Calcium (mg/dL)</td>
<td>9.3</td>
<td>7.2</td>
<td>7.2</td>
<td>8.2</td>
<td>8.5</td>
<td>9.4</td>
<td>9.7</td>
<td>9.3</td>
</tr>
<tr>
<td>Protein (g/dL)</td>
<td>7.3</td>
<td>n/a</td>
<td>n/a</td>
<td>4.6</td>
<td>4</td>
<td>4.5</td>
<td>4.9</td>
<td>5.3</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>5.5</td>
<td>0.8</td>
<td>2.3</td>
<td>1.8</td>
<td>4.2</td>
<td>2.1</td>
<td>4.3</td>
<td>3.9</td>
</tr>
<tr>
<td>Magnesium (mg/dL)</td>
<td>1.6</td>
<td>1.4</td>
<td>1.7</td>
<td>1.9</td>
<td>1.6</td>
<td>1.6</td>
<td>1.9</td>
<td>1.8</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.2</td>
<td>n/a</td>
<td>n/a</td>
<td>2.3</td>
<td>1.9</td>
<td>2.4</td>
<td>2.4</td>
<td>2.3</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>1.1</td>
<td>n/a</td>
<td>n/a</td>
<td>2.4</td>
<td>1.9</td>
<td>1.8</td>
<td>2.3</td>
<td>4.1</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/L)</td>
<td>46</td>
<td>n/a</td>
<td>46</td>
<td>34</td>
<td>47</td>
<td>67</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Aspartate aminotransferase (U/L)</td>
<td>11</td>
<td>n/a</td>
<td>180</td>
<td>184</td>
<td>108</td>
<td>94</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase (U/L)</td>
<td>18</td>
<td>n/a</td>
<td>44</td>
<td>52</td>
<td>40</td>
<td>41</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.3</td>
<td>7.27</td>
<td>7.24</td>
<td>7.42</td>
<td>7.3</td>
<td>7.48</td>
<td>7.42</td>
<td>7.54</td>
</tr>
<tr>
<td>Partial pressure of oxygen (mm Hg)</td>
<td>124</td>
<td>149</td>
<td>84</td>
<td>79</td>
<td>47</td>
<td>154</td>
<td>180</td>
<td>93</td>
</tr>
<tr>
<td>Partial pressure of carbon dioxide (mm Hg)</td>
<td>26</td>
<td>21</td>
<td>43</td>
<td>41</td>
<td>50</td>
<td>31</td>
<td>41</td>
<td>32</td>
</tr>
<tr>
<td>Oxygen saturation (%)</td>
<td>98.1</td>
<td>98.9</td>
<td>94.6</td>
<td>99.3</td>
<td>77.2</td>
<td>99.4</td>
<td>99.3</td>
<td>98</td>
</tr>
<tr>
<td>White blood cells (K/uL)</td>
<td>14.3</td>
<td>n/a</td>
<td>24.7</td>
<td>n/a</td>
<td>33.8</td>
<td>26.5</td>
<td>27.4</td>
<td>23.4</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>13.4</td>
<td>n/a</td>
<td>11</td>
<td>11.5</td>
<td>10.5</td>
<td>9</td>
<td>8.5</td>
<td>8.8</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>39.4</td>
<td>n/a</td>
<td>33.4</td>
<td>34.1</td>
<td>31.2</td>
<td>26.6</td>
<td>24.8</td>
<td>25.4</td>
</tr>
<tr>
<td>Platelets (K/uL)</td>
<td>307</td>
<td>n/a</td>
<td>159</td>
<td>n/a</td>
<td>63</td>
<td>68</td>
<td>84</td>
<td>91</td>
</tr>
<tr>
<td>Creatine phosphokinase (U/L)</td>
<td>46</td>
<td>57</td>
<td>296</td>
<td>2547</td>
<td>5035</td>
<td>2189</td>
<td>1457</td>
<td>1191</td>
</tr>
</tbody>
</table>
New blood test detects colon cancer before it develops

A new blood test developed in the Gastrointestinal Cancer Research Lab at Baylor Research Institute (BRI) is showing very promising results for finding cancer-related microRNA in the blood before a tumor develops in the colon. In a seminal study published in the *Journal of the National Cancer Institute*, the BRI investigators studied several hundred patients with colorectal polyps and cancers and reported that measuring levels of miR-21 in the blood could accurately identify up to 92% of patients with colorectal cancer. Not only is this test good for noninvasively identifying patients who already have colorectal cancer, but it can accurately identify up to 82% of patients with advanced colon polyps, which present the highest risk for developing into colorectal cancers several years later.

“The development of this biomarker is highly encouraging because the high mortality rates associated with colorectal cancer are a consequence of late detection of this disease, underscoring the need for improved early detection, prevention, risk assessment, and intervention,” said Ajay Goel, PhD, director of epigenetics and cancer prevention at BRI. Early detection of advanced colorectal polyps and cancers is considered the most relevant target for screening strategies and the best approach to improving survival of these patients.

“This blood-based test could be transformative in how we screen patients for colorectal cancer; it would save lives and could result in major savings of health care dollars,” said Michael A. E. Ramsay, MD, president of BRI.
RECENT GRANTS

- **Analysis and dissemination of patient-centered outcomes and its impact on patients**
  
  Principal investigator: Ian McCarthy, PhD
  
  Sponsor: Agency for Healthcare Research and Quality
  
  Funding: $145,259
  
  Award period: 7/1/2013–6/30/2014

- **Systems biology of cardiovascular biomarkers in psoriasis**
  
  Principal investigator: Gerlinde Obermoser, MD
  
  Sponsor: National Psoriasis Foundation
  
  Funding: $100,000
  
  Award period: 6/15/2013–6/15/2014

- **Dendritic cell asialoglycoprotein receptor as a novel target for controlling graft-versus-host disease and allograft rejection**
  
  Principal investigator: Sangkon Oh, PhD
  
  Sponsor: National Institutes of Health
  
  Funding: $368,480
  
  Award period: 6/1/2013–6/30/2014

- **Controlling allergen-specific Th2-type responses by targeting dendritic cell surface lectins**
  
  Principal investigator: Sangkon Oh, PhD
  
  Sponsor: National Institutes of Health
  
  Funding: $232,885
  
  Award period: 7/1/2013–6/30/2014

- **Systems analysis vaccine responses in healthy and hyporesponsive humans**
  
  Principal investigator: A. Karolina Palucka, MD
  
  Sponsor: National Institutes of Health
  
  Funding: $3,059,835
  
  Award period: 7/1/2013–6/30/2014

- **North Texas Hepatitis B Consortium: clinical site for the Hepatitis B Network**
  
  Principal investigator: Robert Perrillo, MD
  
  Sponsor: The University of Texas Southwestern Medical Center
  
  Funding: $114,527
  
  Award period: 6/1/2013–5/31/2014

- **Novel treatment and screening strategies in heritable gamma-hydroxybutyric aciduria**
  
  Principal investigator: Lawrence Sweetman, PhD
  
  Sponsor: Washington State University/ National Institutes of Health
  
  Funding: $138,839
  
  Award period: 12/1/2012–11/30/2013

- **National Psoriasis Foundation medical research fellowship program 2013**
  
  Principal investigator: Alan Menter, MD
  
  Sponsor: National Psoriasis Foundation
  
  Funding: $40,000
  
  Award period: 7/1/2013–6/30/2014

- **Implementing a bundle for intensive care unit delirium—the IBID project**
  
  Principal investigator: Andrew Masica, MD
  
  Sponsor: Agency for Healthcare Research and Quality
  
  Funding: $291,506
  
  Award period: 7/1/2013–6/30/2014

- **Harnessing human dendritic cell subsets for improved mucosal vaccines**
  
  Principal investigator: Yong-Jun Liu, MD
  
  Sponsor: National Institutes of Health
  
  Funding: $4,177,256 (fully funded at $4,362,911)
  
  Award period: 5/1/2013–4/30/2014

- **JC virus and human colorectal neoplasia**
  
  Principal investigator: C. Richard Boland, MD
  
  Sponsor: National Institutes of Health
  
  Funding: $120,319 (6-month; fully funded at $251,332)
  
  Award period: 2/1/2013–1/31/2014

- **Familial and early onset colorectal cancer**
  
  Principal investigator: C. Richard Boland, MD
  
  Sponsor: National Institutes of Health
  
  Funding: $78,140 (3-month; fully funded at $312,561)
  
  Award period: 5/1/2013–4/30/2014

- **New-onset post-CABG atrial fibrillation**
  
  Principal investigator: Giovanni Filardo, PhD
  
  Sponsor: National Institutes of Health
  
  Funding: $672,982 (fully funded at $711,867)
  
  Award period: 5/1/2013–4/30/2014

health care professionals and caregivers to learn more about improving care of the older adult.

- **Partnership with nursing homes.** Through partnerships with three nursing homes in Garland and three nursing homes in Irving, Baylor nurses monitor patients’ conditions after discharge and offer education to the staff. Jobeth Pilcher, EdD, RN-BC, explained that Baylor “is starting to see a decrease in readmission rates at those nursing homes.”

- **Transitional care model.** When elderly patients who suffer the effects of heart failure and pneumonia are discharged from a Baylor facility, caregivers follow up with them after 30 days, either in person or on the phone, to check on their condition, answer questions, and ensure that they are adhering to treatment regimens.

- **Inpatient geriatric volunteer program combating delirium**

- **School of nursing consortium**

To share the knowledge they have gleaned with a broader audience, Baylor’s Center for Learning Innovation and Practice sponsored a 2-day interprofessional conference in June: the 2013 Care of the Older Adult: Real World Applications. The conference attracted more than 200 attendees from 12 states. In addition to featuring prominent speakers, the conference introduced its audience to some unique applications of assistive and learning technologies, including a glow-in-the-dark toilet seat, a talking pill dispenser, and a GPS device that alerts when an elderly family member wanders off. “These kinds of assistive technologies offer some pretty creative solutions to tackling the real-world challenges of aging,” said Pilcher.

- **Baylor Medical Center at Frisco expands emergency department**

  Baylor Medical Center at Frisco opened its newly expanded emergency department in August 2013, which more than tripled the emergency department’s footprint with a total of 9031 square feet. It is located on the east side of the main hospital campus. “We’re expanding to meet the growing demand for emergent care in Frisco,” said William Keaton, CEO of Baylor Frisco. “As Frisco remains one of the fastest-growing communities in the nation, keeping our low ‘door-to-doc’ time is a priority we take very seriously.”

- **Study tests new treatment for high-risk patients with aortic stenosis**

  Robert Stoler, MD, FACC, FSCAI, director of the cardiac catheterization lab at Baylor...
Blood secured to a flexible, self-expanding tissue with “leaflets” that control the flow of heart. The artificial valve is made of natural aortic valve via a catheter threaded up to the femoral artery and delivering the new valve frame for support. Patients who have received the system report an immediate improvement in their ability to breathe deeply, and typical recovery time is between 4 and 7 days. Dr. Stoler has high hopes that the CoreValve clinical trial will result in its Food and Drug Administration approval for use in high-risk or inoperable patients within the next 1 to 2 years. He also anticipates that a successful trial will lead to new generations of valves from Medtronic and other device companies coming to trial as advances in the understanding of this treatment continue.

**UPCOMING CME PROGRAMS**

The A. Webb Roberts Center for Continuing Education of Baylor Health Care System is offering the following programs:

- **40th Annual Williamsburg Conference on Heart Disease**, December 8–10, 2013
- **Cardiac Innovations**, May 8, 2014
- **Fifth Annual Latest Advances in Ischemic and Hemorrhagic Stroke Therapy**, May 17, 2014

For more information, call 214-820-2317 or visit www.cmebaylor.org.

**PHILANTHROPY NOTES**

- **NFL lineman goes on the offense for the 14th annual Celebrating Women luncheon**

  The 14th annual Baylor Health Care System Foundation Celebrating Women luncheon will be held on Wednesday, October 23, at 11:45 AM at the Hilton Anatole Hotel in Dallas. The event, presented for the ninth consecutive year by Tom Thumb, has raised more than $19 million to fight breast cancer throughout BHCS. In the past 13 years, donations to Celebrating Women have supported expanded technology, community outreach, innovative clinical research, education, and programmatic needs for the men and women fighting this disease.

  This year’s speaker, Chris Spielman, is an ESPN college football analyst with a remarkable athletic record. An 11-year veteran in the NFL, he is a member of the College Football Hall of Fame, a four-time Pro Bowl linebacker, and a two-time defensive MVP for the Detroit Lions. He discovered after his late wife Stefanie’s diagnosis that his biggest opponent in life wasn’t a hard-hitting football player but the difficult fight against breast cancer. Through his awareness and fundraising work, Chris remains committed to continuing Stefanie’s legacy of hope and to finding a cure.

  For information about underwriting opportunities and tickets to Celebrating Women, call 214-820-4500 or e-mail CelebratingWomen@BaylorHealth.edu. Sponsorship and underwriting opportunities are still available; individual tickets start at $250 and table prices start at $2500.

- **Grand Rounds® Golf Tournament to raise money for medical education**

  D. A. Weibring will be the guest speaker at the VIP celebrity reception for the 12th annual Grand Rounds® Golf Tournament. Golfer, designer, and businessman, D. A. is the founder and chairman of Weibring-Wolfard Golf Design and a full-time player on the PGA Champions Tour. In a career that spans 35 years, D. A. has 13 victories worldwide, including several on the PGA Tour and Champions Tour.

  The event, presented by Bank of Texas and held Monday, October 7, at Dallas’ Northwood Club, raises funds to provide medical education to both undergraduate medical students and graduate physicians at BUMC. Last year, more than 200 golfers and 50 sponsors raised a record $305,000 for the medical education program at BUMC.

  BUMC trains nearly 220 residents and fellows in 30 specialty and subspecialty programs. With donor support, BHCS Foundation plans to fund 30 residents and fellows at a cost of more than $2.2 million this fiscal year. Playing spots and sponsorships for this year’s tournament are now available. For more information, contact Lindsay Nahoum at 214-820-7734 or Lindsay.Nahoum@BaylorHealth.edu.

- **Walk your way to better health at fourth annual DHWI Healthy Harvest event**

  Join us and be a part of the fourth annual Diabetes Health and Wellness Institute (DHWI) Healthy Harvest Fun Walk/5K Run & Diabetes Expo on Saturday, October 26, 2013. The event will bring more than 1000 walkers and runners together at DHWI headquarters to promote awareness and raise funds for the programs at DHWI.

  The event’s keynote speaker is Sherri Shepherd. The host of The View, New York Times best-selling author, and former Dancing with the Stars contestant is dedicated to sharing her passion for staying healthy. DHWI is the area’s first and only diabetes health and wellness facility addressing the region’s health care needs relative to diabetes. The goal of the center is to weave diabetes prevention into the fabric of the community so that it is a natural and convenient part of life in the neighborhood. The mission: To improve the care and save lives of people with diabetes through a new care model focused on health care, education, and research.

  For more information, contact Courtney Brown at 214-820-7410 or Courtney.Brown@baylorhealth.edu.
Baylor expands low-dose CT scan program for those at high risk of developing lung cancer

For people at high risk of developing lung cancer, the most effective screening may be a low-dose CT scan, according to the latest research published from the National Lung Screening Trial in The New England Journal of Medicine. People who are referred by their physician for being at high risk for lung cancer can take advantage of the low-dose CT lung cancer screening at Baylor Charles A. Sammons Cancer Centers at Dallas, Irving, and Plano. Candidates for the screening include current and former smokers over the age of 55, people over 50 years old who have smoked the equivalent of one pack per day for 30 years or three packs a day for 10 years, and people with occupational exposure to other carcinogenic agents, including asbestos and diesel fumes. An important consideration for screening is whether the level of individual risk is high enough for screening to be of benefit. A physician referral is required.

Baylor Endocrine Center begins recruiting for long-term diabetes drug study

Baylor Endocrine Center is looking for volunteers to take part in a study to compare the long-term benefits and risks of four widely used diabetes drugs in combination with metformin, the most common first-line medication for treating type 2 diabetes. The study—called GRADE: Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study—will compare drug effects on glucose levels, adverse effects, diabetes complications, and quality of life over an average of nearly 5 years.

GRADE aims to enroll about 5000 patients around the country. Investigators at Baylor Endocrine Center and 36 other study sites are seeking people diagnosed with type 2 diabetes within the past 5 years. They may be taking metformin but not any other diabetes medications. During the study, all participants will take metformin along with a second medication randomly assigned from among four classes of medications approved for use with metformin by the US Food and Drug Administration.

EPA awards area’s first Energy Star to Baylor Fort Worth

Baylor All Saints Medical Center at Fort Worth recently became the first hospital in the Dallas–Fort Worth metroplex to earn Energy Star certification from the US Environmental Protection Agency. Energy Star certification recognizes the hospital for its leadership in energy management and conservation efforts.

Key elements of Baylor Fort Worth’s energy management strategy included upgrading older HVAC equipment to improve efficiency; replacing parking garage light fixtures with new, more efficient lighting; creating an operational efficiency scorecard for engineering focusing on identifying, implementing, and measuring energy improvements in daily facility operations; and launching an employee energy awareness program.

Results of the program since July 2010 include $825,000 in energy project savings; a 12.4% year-over-year reduction in total energy consumption; a 9.5% year-over-year reduction in water consumption; an 11.1% commingled recycle rate; and a 52% overall improvement in first-year operational energy scorecard performance.

Providing a new dimension to medical care: the Integrative Medicine Program at Baylor Charles A. Sammons Cancer Center at Dallas

The Integrative Medicine Program at Baylor Charles A. Sammons Cancer Center at Dallas—the first hospital-based program in North Texas—offers different therapies that work together with traditional medicine to help patients. The program focuses on each patient’s concerns from a holistic viewpoint and addresses nutritional, physical, emotional, and spiritual aspects of their lives.

“Every patient is unique, and individual recommendations are tailored for the patient’s own set of circumstances and concerns,” said Carolyn Matthews, MD, a gynecologic oncologist on the medical staff at BUMC and medical director of the Integrative Medicine Program. “In the last year, we have helped patients fine-tune their lifestyles to address such issues as weight loss, hypertension, and chronic back pain, in addition to helping those patients being treated for cancer.” Dr. Matthews is board certified in integrative and holistic medicine, medical acupuncture, and palliative medicine.

Therapies include nutritional guidance, with a focus on special diets and botanical supplements, as well as mind-body techniques such as acupuncture. Guided imagery, breathing for stress relief and relaxation, and personalized exercise programs are also offered as part of integrative therapies. Music and art classes also add dimension to customized care plans. Cooking classes focusing on the nutritional needs of patients during treatment are offered in an on-site demonstration kitchen, a program that is unique to Baylor Sammons Cancer Center. The integrative medicine program works in conjunction with the Virginia R. Cvetko Patient Education and Support Center.

“Integrative medicine contributes to all the incredible advances made in traditional medicine,” said Dr. Matthews. “This is a way to supplement or integrate existing treatment options with ‘low-tech’ approaches, some of which have been around for thousands of years.”

Two Baylor hospitals recognized among best in nation for heart surgery

Baylor Heart and Vascular Services at Dallas and The Heart Hospital Baylor Plano have earned the coveted 3-star rating from the Society of Thoracic Surgeons (STS). The rating—the highest honor bestowed by STS—is for both aortic valve replacement surgery and heart bypass surgery. Less than 3% of the nation’s hospitals have earned 3-star ratings. The STS National Cardiac Database, which the STS rating system is based upon, measures outcomes for more than 90% of the 1100 cardiac surgery programs in the United States.

“Only 24 hospitals in the US are STS 3-star hospitals in both procedures. Baylor is home to two of them,” says Michael Mack, MD, FACS, medical director of cardiovascular disease for BHCS. “I think that’s an exclamation point on our long-standing commitment to improving the quality of care for patients with heart disease and striving to offer a level of medical excellence that just isn’t available everywhere.”

Providing a new dimension to medical care: the Integrative Medicine Program at Baylor Charles A. Sammons Cancer Center at Dallas

The Integrative Medicine Program at Baylor Charles A. Sammons Cancer Center at Dallas—the first hospital-based program in North Texas—offers different therapies that work together with traditional medicine to help patients. The program focuses on each patient’s concerns from a holistic viewpoint and addresses nutritional, physical, emotional, and spiritual aspects of their lives.

“Every patient is unique, and individual recommendations are tailored for the patient’s own set of circumstances and concerns,” said Carolyn Matthews, MD, a gynecologic oncologist on the medical staff at BUMC and medical director of the Integrative Medicine Program. “In the last year, we have helped patients fine-tune their lifestyles to address such issues as weight loss, hypertension, and chronic back pain, in addition to helping those patients being treated for cancer.” Dr. Matthews is board certified in integrative and holistic medicine, medical acupuncture, and palliative medicine.

Therapies include nutritional guidance, with a focus on special diets and botanical supplements, as well as mind-body techniques such as acupuncture. Guided imagery, breathing for stress relief and relaxation, and personalized exercise programs are also offered as part of integrative therapies. Music and art classes also add dimension to customized care plans. Cooking classes focusing on the nutritional needs of patients during treatment are offered in an on-site demonstration kitchen, a program that is unique to Baylor Sammons Cancer Center. The integrative medicine program works in conjunction with the Virginia R. Cvetko Patient Education and Support Center.

“Integrative medicine contributes to all the incredible advances made in traditional medicine,” said Dr. Matthews. “This is a way to supplement or integrate existing treatment options with ‘low-tech’ approaches, some of which have been around for thousands of years.”

Two Baylor hospitals recognized among best in nation for heart surgery

Baylor Heart and Vascular Services at Dallas and The Heart Hospital Baylor Plano have earned the coveted 3-star rating from the Society of Thoracic Surgeons (STS). The rating—the highest honor bestowed by STS—is for both aortic valve replacement surgery and heart bypass surgery. Less than 3% of the nation’s hospitals have earned 3-star ratings. The STS National Cardiac Database, which the STS rating system is based upon, measures outcomes for more than 90% of the 1100 cardiac surgery programs in the United States.

“Only 24 hospitals in the US are STS 3-star hospitals in both procedures. Baylor is home to two of them,” says Michael Mack, MD, FACS, medical director of cardiovascular disease for BHCS. “I think that’s an exclamation point on our long-standing commitment to improving the quality of care for patients with heart disease and striving to offer a level of medical excellence that just isn’t available everywhere.”
Clinical research studies enrolling patients through Baylor Research Institute

Currently, Baylor Research Institute is conducting more than 800 research projects. Studies open to enrollment are listed in the Table. To learn more about a study or to enroll patients, please call or e-mail the contact person listed.

<table>
<thead>
<tr>
<th>Research area</th>
<th>Specific disease/condition</th>
<th>Contact information (name, phone number, and e-mail address)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma and pulmonary disease</td>
<td>Chronic obstructive pulmonary disease, asthma (adult)</td>
<td>Rose Boehm, CCRC, RRT, RCP 214-820-9772 <a href="mailto:RoseB@BaylorHealth.edu">RoseB@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Cancer</td>
<td>Breast, ovarian, endometrial, prostate, brain, lung, bladder, colorectal, pancreatic, and head and neck cancer; hematological malignancies, leukemia, multiple myeloma, non-Hodgkin’s lymphoma; melanoma vaccine</td>
<td>Grace Townsend 214-818-8472 <a href="mailto:cancer.trials@BaylorHealth.edu">cancer.trials@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Diabetes (Dallas)</td>
<td>Type 1 and type 2 diabetes, cardiovascular events</td>
<td>Kris Chionh 214-820-3416 <a href="mailto:kristen.chionh@BaylorHealth.edu">kristen.chionh@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Diabetes (Fort Worth)</td>
<td>Type 2; cardiac events</td>
<td>Trista Bachand, RN 817-922-2587 <a href="mailto:trista.bachand@baylorhealth.edu">trista.bachand@baylorhealth.edu</a></td>
</tr>
<tr>
<td>Gastroenterology</td>
<td>Crohn’s disease</td>
<td>Dallas Clinical Trials Office 214-820-9626 <a href="mailto:kristen.chionh@baylorhealth.edu">kristen.chionh@baylorhealth.edu</a></td>
</tr>
<tr>
<td>Heart and vascular disease (Dallas)</td>
<td>Aortic aneurysms, coronary artery disease, hypertension, poor leg circulation, heart attack, heart disease, congestive heart failure, angina, carotid artery disease, familial hypercholesterolemia, surgical renal denervation for hypertension, diabetes in heart disease, cholesterol disorders, heart valves, thoracicotomy pain, stem cells, critical limb ischemia, cardiac surgery associated with kidney injury</td>
<td>Merielle Boatman 214-820-2273 <a href="mailto:MeriellH@BaylorHealth.edu">MeriellH@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Heart and vascular disease (Fort Worth)</td>
<td>Atrial fibrillation, carotid artery stenting</td>
<td>Deborah Devin 817-922-2575 <a href="mailto:Deborah.Devlin@BaylorHealth.edu">Deborah.Devlin@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Heart and vascular disease (Plano)</td>
<td>Aneurysms; coronary artery disease; surgical renal denervation, or stent, for uncontrolled hypertension; poor leg circulation; heart attack; heart disease; heart valve repair and replacement; critical limb ischemia; repair of AAA, TAA, and dissections with endografts; thoracic surgery leak repair; atrial fibrillation; carotid artery disease; congestive heart failure; left atrial appendage and stroke; gene profiling</td>
<td>Natalie Settele, PA-C 469-814-4712 <a href="mailto:natalie.settele@BaylorHealth.edu">natalie.settele@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Hepatology</td>
<td>Liver disease</td>
<td>Cheryl Sandbach 214-820-6267 <a href="mailto:cheryl.sandbach@BaylorHealth.edu">cheryl.sandbach@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Infectious disease</td>
<td>HIV/AIDS</td>
<td>Bryan King, LVN 214-823-2533 <a href="mailto:bryan.king@ntidc.org">bryan.king@ntidc.org</a></td>
</tr>
<tr>
<td>Infectious disease</td>
<td>Hepatitis C, hepatitis B</td>
<td>Cheryl Sandbach 214-820-6267 <a href="mailto:cheryl.sandbach@BaylorHealth.edu">cheryl.sandbach@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Nephrology</td>
<td>Homocysteine and kidney disease, dialysis fistulas, urine/protein disorders in cancer patients</td>
<td>Dallas Clinical Trials Office 214-820-9626 <a href="mailto:Kristen.chionh@BaylorHealth.edu">Kristen.chionh@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Neurology</td>
<td>Stroke</td>
<td>Dion Graybeal, MD 214-820-4561 <a href="mailto:Dion.Graybeal@BaylorHealth.edu">Dion.Graybeal@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Neurology</td>
<td>Multiple sclerosis</td>
<td>Annette Okai, MD 214-820-4655 <a href="mailto:annette.okai@BaylorHealth.edu">annette.okai@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>Cerebral aneurysms</td>
<td>Kenneth Layton, MD 214-827-1600 <a href="mailto:KenelinL@BaylorHealth.edu">KenelinL@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Rheumatology (9900 N. Central Expressway)</td>
<td>Rheumatoid arthritis, psoriatic arthritis, lupus, gout, ankylosing spondylitis</td>
<td>John J. Cuth, MD 214-987-1253 <a href="mailto:jennihal@BaylorHealth.edu">jennihal@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Rheumatology (9900 N. Central Expressway)</td>
<td></td>
<td>Kathryn Dao, MD 214-987-1249 <a href="mailto:jennihal@BaylorHealth.edu">jennihal@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Transplantation</td>
<td>Bone marrow, blood stem cells</td>
<td>Grace Townsend 214-818-8472 <a href="mailto:Grace.Townsend@BaylorHealth.edu">Grace.Townsend@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Transplantation</td>
<td>Solid organs</td>
<td>Jonnie Edwards 214-820-6243 <a href="mailto:jonnie.edwards@baylorhealth.edu">jonnie.edwards@baylorhealth.edu</a></td>
</tr>
<tr>
<td>Weight management</td>
<td>Obesity</td>
<td>Kris Chionh 214-820-3416 <a href="mailto:kristen.chionh@BaylorHealth.edu">kristen.chionh@BaylorHealth.edu</a></td>
</tr>
<tr>
<td>Women’s health (Fort Worth)</td>
<td>Endometriosis and endometrial ablation; interstitial cystitis/bladder pain syndrome</td>
<td>Theresa Cheyne, RN 817-922-2579 <a href="mailto:theresa.cheyne@BaylorHealth.edu">theresa.cheyne@BaylorHealth.edu</a></td>
</tr>
</tbody>
</table>

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.
The very existence of ethics consultation reflects both the increasing complexity of modern medicine’s ethical questions and our discomfort with the prospect of answering them alone. Two developments in the past century were instrumental in driving the development of ethics consultation—organ replacement therapy and intensive care. With the proliferation of extreme life-prolonging measures came the thorny difficulties in the withdrawal of such services or rationing when resources were poor. Insofar as “someone must,” lamented Dr. Karen Teel (a pioneer of ethics consultation), the physician “is charged with the responsibility of making ethical judgments which we are sometimes ill-equipped to make.” More than anything, ethics consultation has come to best satisfy a central desire of American health care—sharing the responsibility for tough decisions.

Today, ethics consultants are an important component of American health care delivery. They are found in 81% of hospitals and 100% of those with more than 400 beds. In one year (2006), 29,000 individuals performed 36,000 consultations, devoting 314,000 hours (1). By one account, ethics consultations are performed for 0.16% of all hospital admissions (2). In a relatively short time, a novel discipline has emerged and thrived in American hospital wards.

Born to serve the dual and reinforcing fears of futile care and medicolegal liability, the ethics consult has come to reflect both the increasing complexity of medicine’s ethical questions and our discomfort with the prospect of answering them alone. The practice of ethics consultation developed slowly in the 1970s and 1980s, was essentially fully formed by 1987, and has proliferated since. It is now nearly ubiquitous (1). Then, as now, the matters of standards, credentials, and how we evaluate consultation are very controversial. Yet, despite the lack of clarity about fundamental aspects of this enterprise, ethics consultation flourishes. More than anything, ethics consultation has come to best satisfy a central desire of American health care—sharing the responsibility for tough decisions. Herein, this historical study of ethics consultation examines the practice’s roots, the forces that shaped it, and the people responsible for its development.

MEDICAL ETHICS

Clinical ethics consultation is a relatively novel service that developed within the broader history of medical ethics. The history of contemporary medical ethics—rich, broad, and mostly outside the bounds of this inquiry—began in 1802. Thomas Percival, an English physician, coined the term “medical ethics” in a widely circulated pamphlet wherein he unilaterally codified the professional ethic of doctors. The Percivillian code—which formed the basis for the American Medical Association’s code of ethics—asserted the moral authority and independence of physicians in service to others, affirmed the profession’s responsibility to care for the sick, and emphasized individual honor (3). The rigorous study of how this code translated to practice began in earnest as recently as the 1950s. Joseph Fletcher’s *Morals and Medicine* (1954) was the first major work to closely examine the “knotty issues” of medicine, old (e.g., euthanasia) or new (e.g., artificial insemination) (3, 4). Fifteen years later, Paul Ramsey, a theologian, was the first to lay out a systematic approach to these issues that became known as bioethics. As he wrote in his seminal work, *The Patient as a Person* (1970), “I could put my questions to experts in many fields of medicine, overhear discussions among them, and begin to learn how teachers of medicine . . . themselves understand the moral aspects of their practice” (5, 6). Meanwhile, the discussion that Paul Ramsey began in the academy was slowly developing in the clinic. In 1949, Catholic hospitals began forming “mediomoral committees” to discuss and maintain Catholic values in health care delivery (7). The concept of an ethics committee, however, was slow to take a widespread hold.

THE PHYSICIAN’S DILEMMA AND THE ETHICS COMMITTEE

Notwithstanding the infancy of medical ethics, medical technology—and with it the scope and reach of medical interventions—was advancing spectacularly. By the mid 20th century, there were several signs that medical technology had outstripped the capacity of individual physicians to confidently navigate clinical medicine’s ethical quandaries. Two developments were instrumental—organ replacement therapy and...
intensive care. Together, they led directly to the formation of ethics committees and, later, ethics consultation.

In 1960, Belding Scribner’s Teflon arteriovenous shunt enabled outpatient hemodialysis for the first time. Immediately, there was far more demand for this procedure than supply. Concerned about fairness in rationing, the Seattle Artificial Kidney Center founded an “Admissions and Policy Committee.” Composed of a minister, a lawyer, a businessman, a homemaker, a labor leader, and two physicians, this committee chose the patients who received the available dialysis slots. Shana Alexander, the journalist who immortalized the so-called “God-Squad” in her blockbuster Life magazine article, declared that “they decide who lives, who dies.” A central theme in her interviews was the need to share in the responsibility of such weighty decisions. Indeed, Alexander sympathized with the hospital, arguing that “the medical fraternity should share the burden [of these decisions] . . . otherwise society would be forcing the doctors alone to play God” (8).

Dialysis and, later, the advent of renal transplantation raised the stakes on medical decisions at the end of life, for both those patients with and without a chance for survival. Accordingly, in 1968, Harvard famously commissioned a committee to provide a “definition of irreversible coma” (9). The fact of this report on “brain death” spoke not only to the problem of organ supply and determining from which bodies it is appropriate to harvest organs but also generalized difficulties in knowing when to terminate “life support.” As they wrote, “Obsolete criteria for the definition of death can lead to controversy in obtaining organs for transplantation.” At the same time, intensive care or “improvements in resuscitative and supportive measures have led to increased efforts to save those who are desperately injured.” These efforts place a difficult burden on patients, “on their families, on the hospitals and on those in need of hospital beds already occupied by these comatose patients” (9).

Indeed, the linchpin in this history is the intensive care unit (ICU) and the technical advancements thereof. With the proliferation of extreme life-prolonging measures came the difficulties in the withdrawal of such services. In the context of a litigious society, a worry quickly developed about the consequences in withdrawing life support. There was a pervasive sense that physicians were duty bound to provide universal cardiopulmonary resuscitation and support. These were procedures whose benefit was a given, and thus the failure to provide them “might invite civil suits or criminal prosecution” (10). It was easy to start life support but stopping it or withholding it proved trickier. Patients were just as uneasy with life support. In 1969, the first “living will” emerged and slowly gained popularity (11).

End-of-life decisions in the ICU took on a fundamentally legalistic character which, in turn, led to the creation of ethics committees. Dr. Karen Teel, a pediatrician at the Children’s Hospital of Austin, saw physicians “faced with the reality of a no-win situation.” Insofar as “someone must,” the physician “is charged with the responsibility of making ethical judgments which we are sometimes ill-equipped to make.” “In good faith, he acts,” “assuming a civil and criminal liability.” Teel referred to the “God Squad” (as Seattle’s committee was known colloquially) and argued that all hospitals ought to provide a mechanism to share in the responsibility of such tough decisions, one that would “provide a regular forum for more input and dialogue in individual situations and . . . allow the responsibility for these judgments to be shared.” Crucially, she published these thoughts in a 1975 article entitled “A Physician’s Dilemma” in a law review journal (12).

As it happens, shortly thereafter, the Karen Ann Quinlan legal saga was coming to a close. As a frail college student in New Jersey, Ms. Quinlan aspirated after an accidental over-dose of benzodiazepines and alcohol, resulting in a persistent vegetative state. Her parents eventually decided to terminate ventilation. Her doctors, however, worried about the implications and resisted. The result was a definitive, landmark legal battle. Judge Richard J. Hughes presided and ruled the extubation legally sound. And in setting this precedent, he cited Teel, urging all hospitals to adopt her proposal for an ethics committee (13).

Ethics committees appeared around the country but were not successful in addressing their motivating concerns. The Beth Israel Hospital in Boston was a leader, forming an ad hoc committee of physicians and nurses to help treating physicians determine if a “do-not-resuscitate” order was appropriate for those patients who were competent to choose and not “irreversibly and irreparably ill” (14). It could be left to the physician alone to discuss the order with the committee, if the patient was, in fact, irreparably ill. This committee indirectly addressed the fear of litigation by sharing responsibility. Above all, it served to mitigate for treating physicians the feelings of guilt and uncertainty bound up in forgoing resuscitative measures (personal correspondence, Dr. Rabkin). Across town, the Massachusetts General Hospital organized the “Optimum Care Committee” to address the care of the hopelessly ill patient and the utilization of critical care resources. Its mandate, far more expansive than Beth Israel’s, was to determine “what would be the best thing to do for the patient” (15). Controversy followed with many unanswered philosophical questions: To what end? In whose service? Who joins? What sort of background was required for membership? (16, 17).

No one had satisfactorily addressed the concerns of conflict of interest and authority before the fact of the committee, let alone what an ethics committee would actually do on a day-to-day basis. This had practical consequences. For example, the ethics committee at Montefiore Medical Center was established in 1977, quickly became a “discussion group,” and floundered “because of lack of clear direction well into the 1980s” (18). Furthermore, there remained a widespread concern that the removed committee was an inappropriate mechanism to solve the dilemmas of the bedside (17). Five years into the committee era, the fear of legal liability had only worsened. One observer remarked, “It has become almost impossible for some classes of patient to die without a court order” (19). Hospitals began deliberately choosing to not start new committees (20). In 1982, only 1% of US hospitals had adopted ethics committees (21). The physician’s dilemma persisted.
“PSYCHIATRIC CONSULTATION MASKING MORAL DILEMMAS IN MEDICINE”

Confronting modern ethical dilemmas alone at the bedside, clinicians yearned for support. For this, they often turned to psychiatrists, asking consultants to weigh in on what turned out to be fundamentally ethical troubles. Clinicians began using the accessible language of psychiatry to frame their dilemmas. Dr. Mark Perl, a psychiatrist, exposed this practice with a case series in the *New England Journal of Medicine*. One patient with metastatic osteosarcoma refused treatment. Her oncologist consulted Perl for “the clinician’s desires” (22). There was a growing demand for a consultant to sort out clinical ethical questions.

Mark Perl, a psychiatrist, exposed this practice with a case series in the *New England Journal of Medicine*. One patient with metastatic osteosarcoma refused treatment. Her oncologist consulted Perl for “the clinician’s desires” (22). There was a growing demand for a consultant to sort out clinical ethical questions.

THE ETHICISTS

Across the country, a small group of “ethicists” began to offer consultations. Professional ethicists—academics trained in various disciplines of the humanities—were increasingly available on hospital campuses. Largely, they were teachers of medical students, asked to guide students through the ethical questions engendered by the modern physician’s dilemma. Indeed, the proliferation of ethicists occurred concomitantly with the above developments during the 1970s: in 1972, 4.2% of medical schools had formal medical ethics curricula, and by 1982, 72.8% did; that percentage has remained about the same (78% in 2004) (23, 24). The pioneers of the field at this time included John Fletcher (philosopher; National Institutes of Health), William Winslade (lawyer and psychoanalyst; University of California at Los Angeles), John Golensky (minister; California), Ruth Macklin (philosopher; Albert Einstein), among many others. Foremost in this group was the philosopher Albert Jonsen. It is likely that he was the first ethicist at the bedside sometime in the early 1970s at the University of California at San Francisco, where he taught ethics to medical students when Dr. William Tooley (neonatologist) asked Jonsen to initiate bedside teaching in the neonatal ICU (personal correspondence, Dr. Jonsen). Jonsen is also responsible for training many of the most important figures in the field, including Bernard Lo (University of California at San Francisco) and John Golensky. Golensky, in turn, was responsible for developing ethics consultation services in countless hospitals across the nation, including those within the Kaiser Permanente system (personal correspondence, Dr. Golensky). These ethicists were busy and they were in demand.

The first ethics consultation in the published record was conducted by such an ethicist. Dr. Ruth Purtilo, a professor of ethics and physical therapy at the University of Nebraska, published her case in the *New England Journal of Medicine*. The patient was a critically ill neonate with gastrochisis. Her consultation “entailed an in-depth analysis of the moral obligations, rights, responsibilities, and considerations of justice that bear on the infant’s situation” (25). She helped the physicians work through their thoughts, ultimately providing “reassurance that the clinicians had all the pertinent ethical data needed for assessing the ethical problem.” Confirming the problem with committees, she lamented that “in our hospital, most cases in which a clinician can benefit from a sympathetic and skilled ethicist never reach the committee” (25). Consulting ethicists provided one solution to the physician’s dilemma.

CLINICAL ETHICS

Meanwhile, in Chicago, Dr. Mark Siegler became the director of the University of Chicago’s new medical ICU in 1972. Quickly he found that “there was no place to send my housestaff and students to find answers” to the troubling questions engendered by intensive care (26). He was not alone. While increasing numbers of nonmedical academics were specializing in medical ethics, starting journals (*Hastings Center Report*, 1971) and departments (Kennedy Center at Georgetown, 1971), these people were predominantly concerned with theory. There was a critical gap for practicing clinicians seeking guidance in ethics. The Kennedy Center began offering immersion courses in medical ethics. However, in the words of one observer, they were “long discussions on rather esoteric, theoretical and philosophical problems, at the expense of more practical topics of interest to the average physician” (27). The field of biomedical ethics often had little to do with day-to-day medicine. Its “language of theory was not helpful in resolving the dilemmas of practice” (26). Disturbed by “the lack of involvement by physicians” in biomedical ethics, Siegler brought a refocus on physicians and their training to tackle the dilemma (28). This was revolutionary. “It is clear by now,” he observed, “that medicine has merely reacted to, rather than anticipated or participated in, most major developments in biomedical ethics” (28). The medical establishment was trying to divide the clinical from ethical by fostering a class of ethical arbiters. Siegler spoke out against this. “The distinction that is to be made between clinical decisions and ethical ones is an invidious, but unfortunately misguided, one.” The treating physician, ultimately accountable to the patient, cannot “relly on the false courage of the noncombatant” (28). Medicine, more “than a technical service delivered like auto-repair or plumbing,” has inextricably linked technical and ethical dimensions (29).

In 1978, Siegler coined the phrase “clinical ethics” in a paper where he argued that “whatever else medical ethics is, it must have something to do with the practice of clinical medicine” (30). Siegler’s clinical ethics is an approach to the difficult questions of patient care that is a fundamentally bedside procedure, aimed at bedside clinicians. He saw the solution to the “physician’s dilemma” in education and training. He was, from the outset, inspired by the words of Sir William Osler:

In what may be called the natural method of teaching, the student begins with the patient, continues with the patient, and ends his study with the patient, using books and lectures as tools, as means to an end. . . . The best teaching is that taught by the patient himself (30).
Siegler’s model of clinical ethics begins and ends with the patient, its aims derivative of and guided by the patient-doctor relationship. This puts Siegler at odds with the prevailing concept of medical ethics, wherein nonphysicians were providing the bulk of the consultations. Siegler’s vision involves training physicians to conduct ethical medicine and, perhaps, to involve trained physicians as ethics consultants where needed. This conflict has never been resolved but compromises have been made. Thus, in 1980, Siegler joined with Albert Jonsen and William Winslade to draft a pocket guide for clinical ethics aimed at all clinicians. Over 2 weeks, in Jonsen’s house overlooking the San Francisco Bay, they developed the famous “four box method” that importantly orients all ethical discussions to consider first the medical promises have been made. Thus, in 1980, Siegler joined with Albert Jonsen and William Winslade to draft a pocket guide for clinical ethics aimed at all clinicians. Over 2 weeks, in Jonsen’s house overlooking the San Francisco Bay, they developed the famous “four box method” that importantly orientats all ethical discussions to consider first the medical indications, followed by patient preferences, quality of life, and other contingencies. Clinical Ethics (1982) is actually a step-by-step guide to the ethics of medicine organized by clinical scenario. Cases are presented—e.g., “The Problem Patient: Critically Ill”—the ethical dimensions are dissected, and recommendations are made (31). Clinical ethics consultation, provided by a physician or not, now had a process and a manual.

THE SOCIETY FOR BIOETHICS CONSULTATION

By 1985, far from having practice standards, it was still not even clear who should consult or what a consult should look like. To unite the pioneers of consultation, John Fletcher convened a conference on ethics consultation at the National Institutes of Health. Sixty-one people were in attendance; 31 (51%) had PhDs, 8 (13%) had MDs, 8 (13%) had JDs, and 14 had other degrees. Thirty-eight consultants participated in a survey on their practices. Nineteen (53%) kept records in the chart of their consultations, 8 (21%) made medical rounds, and only 11 (29%) were employed by hospitals with ethics committees (32). The most frequent issue encountered was “removal of life support in terminal cases.” Thirty-nine consultants participated in another survey about the conference itself. The group praised the conference for its “sharing of diverse experiences and ideas” and being “the beginning of attention to ethical consultants.” However, there were many criticisms, including a “lack of a formal discussion on what participants actually do with regard to consultation—their roles and aims.” One participant even asked, “Should this breed of technician be encouraged?” The most contentious issue was credentials. Indeed, the attendees were split across this fault line. John Golensky argued that consultants “needed credentials and defined skills,” while Siegler and his fellow, Dr. John La Puma, disagreed. La Puma emerged as the strongest advocate of the physician-as-consultant position. In the end, no compromise could be struck at this meeting (personal correspondence, Dr. Golensky).

Eleven of the participants gathered at the National Institutes of Health in early 1986 and agreed to found the Society for Bioethics Consultation (SBC), the first organization devoted to the subject, and a growing number of textbooks. develop their own training programs. John Fletcher lamented in a memorandum that interested graduate students and professionals had no one to guide them, that "no organized body is working on the problem. . . . Why not us?" The SBC planned three conferences across the nation between September 1987 and March 1988. However, interest was very weak. The lack of cohesiveness at the prior meeting had dampened general enthusiasm for the society. So few had registered, including three of the 61 attendees of the 1985 conference, that all conferences were cancelled (archived memoranda, Moody Medical Library).

THE CLINICAL ETHICIST

In the mid 1980s, a young resident at the West Los Angeles Veteran’s Administration attended a grand rounds on clinical ethics by Dr. Bernie Lo. That resident was Dr. John La Puma. Today he is the “Chef MD.” At the time, he was an ethically minded resident invited to have lunch with Lo. At that lunch, Lo told him about a brand new sort of fellowship getting started up for people like him at the University of Chicago led by Mark Siegler. La Puma left for Chicago after residency as a member of the first class of fellows at Siegler’s MacLean Center for Clinical Ethics (personal correspondence, Dr. La Puma).

During his fellowship, La Puma set up in a community hospital a weekly case conference to discuss clinical ethics with the ward clinicians and covertly promoted and developed his own consult service. Despite his work being informed at every level by Siegler, Siegler himself thought—at least at the time—that ethics consults were intrusive and potentially harmful to the core relationship between the primary doctor and patient. Siegler believed that the primary doctor was the rightful target of clinical ethics education and interventions. Meanwhile, La Puma was working hard to legitimize the practice to his mentor. He collected 27 experiences which dealt, by and large, with finality and the do-not-resuscitate discussion. Then, unbeknownst to Siegler, he published them in the Western Journal of Medicine (33).

Perhaps owing to the strength of its foundations, the method that La Puma employed and reported for his consultations remains essentially unchanged to this day. Two features of the La Puma-Siegler method ought to be highlighted. First, La Puma made sure to expand the social history, asking not how many packs per day but deeper questions about worldview to get at where the patient was coming from. Second, and crucially, unlike Jonsen and Purtilo before him, the consultant would do a physical exam and review laboratory values. True to the “four box method,” La Puma began by reviewing the chart and grounded his recommendations in the medical indications. Borrowing the style and structure of a traditional medical consult, the La Puma-Siegler method lent immediate credibility to the ethics consult.

STANDARDS AND EVALUATION

By 1987, ethics consultation had matured. There was a manual, a published record of experiences, a series of journals devoted to the subject, and a growing number of textbooks.
Little has changed since. Since 1992, the Joint Commission on the Accreditation of Healthcare Organizations has required all of its approved hospitals to construct means for resolving ethical conflicts. In 1996, a consensus statement was preparing describing the aims of consultation:

...a service provided by an individual consultant, team, or committee to address the ethical issues involved in a specific clinical case. Its central purpose is to improve the process and outcomes of patient care by helping to identify, analyze, and resolve ethical problems (34).

In 2000, a joint task force of the SBC and Society for Health and Human Values published the recommendations that nearly crushed the society in 1985. They compromised, recommending that “individual consultants, teams, or committees should have the core competencies for ethics consultation,” that an “evaluation of process, outcomes, and competencies is needed,” but that there “ought not to be any requirement for the certification of individuals and accreditation of programs” (35).

Despite roughly 30 years of service, the issues addressed have not changed, with goals of care and medical futility representing 54%, and withholding or withdrawing measures the focus of 52% of consultations at one center (36). And despite the task force recommendations, only 15% of all consultations had any form of external review of their services (1). Meanwhile, 45% of consultants in one survey reported receiving only informal, on-the-job training, while 73% of consultants at pediatric hospitals reported informal training and 40% worked in hospitals without formal guiding policies (37). The literature still sees calls for studies to identify “indicators that lead to ethics consultation...and the enumeration of the various ethical skills, such as dispute resolution, utilized during ethics consultation” (38).

We are still trying to figure out how to evaluate ethics consultation. In the past two decades, owing to amazing concerted efforts, ethics consultation has been involved in two ambitious multicenter clinical trials, one of which was even randomized. Only one, however, showed that ethics consultation had any effect, measured by resource utilization in patients who would not survive to discharge (39, 40). It is not clear that ethics consultation or committees can or even ought to be evaluated by a randomized trial (41). After all, it is possible that the greatest role of the ethics consultant is the sharing of responsibility, an effect that cannot be measured in patient outcomes.

CONCLUSION

The history of ethics consultation reflects the developments of modern medicine. Ethics consultation is a hospital service providing support for clinicians that developed in response to the practical bedside difficulties inherent to the era of organ replacement/transplantation and brain death. The credibility of ethics consultants will be adjudicated less on the basis of their credentials than on their ability to address Karen T eel’s *physician’s dilemma*—to soothe the anxiety and share the responsibility for difficult medical decisions.

Dental education has gone through numerous changes since World War II. These changes have had, and continue to have, a major impact on the practice of dentistry in the United States and Texas.

NATIONAL TRENDS

Dental schools
In 1950, there were 42 dental schools in the US, 60% of which were affiliated with private universities (Figure 1). With some government assistance and support from a growing applicant pool, the number of dental schools increased to 60 by 1978. Most of this growth was in schools that were affiliated with public universities; they represented 58% of the schools at that time. However, not all these schools were destined to survive. Beginning in the mid 1970s, the dental school applicant pool began a steep decline. By 1989, the number of applicants to dental school had decreased by two thirds. As a direct or indirect result, six of the dental schools closed—all affiliated with private universities. New dental schools began to open shortly after the turn of the century. By fall 2013, the number of fully operational schools had increased to 64. In addition, several universities around the country are in various stages of planning to open a new dental school, although there is a great deal of uncertainty as to the number of these plans that will come to fruition.

Dental school enrollment
As might be expected, dental school enrollment follows a pattern similar to the trend in the number of dental schools. Between 1950 and 1971, there was a steady increase in first-year enrollment in dental schools, totalling 47.1%, or 2.2% per year (Figure 2). The first-year enrollment growth rate then more than doubled between 1971 and 1978—increasing by 32.8%, or 4.7% per year. A significant amount of this growth can be attributed to a federal capitation program that began in 1972. Through this program, the federal government gave dental schools approximately $251.5 million to build new dental schools, renovate existing schools, and increase enrollment. If this amount were adjusted for inflation, it be would close to a billion dollars today. These funds played a crucial role in updating the dental education infrastructure. As enrollment increased, dental school graduates followed (Figure 2). Between 1950 and 1975, the number of dental school graduates increased by 2506 (88.6%).

Enrollment trends generally follow applicant trends; thus, the decline of applicants during the late 1970s and the 1980s had a direct impact on enrollment. First-year enrollment in...
dental school peaked in 1978 at 6301 and then dropped to 3979 in 1989, a decrease of 36.9%. Because of the enrollment build-up, dental school graduates did not begin to fall off until the mid 1980s. Between 1975 and 1984, dental schools graduated more than 5000 dentists a year. By 1990 the number of dental school graduates had dropped to <4000 (3995).

The trend in the number of applicants to dental school reversed, and the number of applicants began to increase in 1990. As a result, between 1989 and 2010, first-year enrollment increased from 3979 to 5171—a 30% increase. Dental school graduates increased by more than 1000, from 3701 in 1994 to 4496 in 2010 (35%). With new schools coming on line and some existing schools increasing their class size, it is likely that enrollments and graduates will continue to increase until at least the middle of the decade.

TRENDS IN TEXAS

In 1970, the University of Texas Health Science Center at San Antonio’s dental school accepted its first class. The University of Texas Dental Branch at Houston and the Baylor College of Dentistry had been around since the turn of the past century (1901). Since 1970, these three schools have been the only dental schools in Texas. During the 1970s and 1980s, enrollment trends in Texas schools mirrored the national trends (Figure 3). During the decade of the 1970s, first-year enrollment in Texas schools almost doubled, increasing from 221 to 417 in 1979. Then, as in the national trend, first-year enrollment fell to 246 in 1993. First-year enrollment levels were relatively flat for the next 10 years; however, since 2004, enrollment has crept up to almost 300. Class sizes at the three schools are currently fairly similar, with each school having a class size of about 100 students. Naturally, the number of graduates of Texas dental schools follows the first-year enrollment trend. The number of graduates increased from 191 in 1970 to 384 in 1985 and then decreased to 228 in 1996. Since then, the number of graduates has remained fairly consistent, increasing to only 258 in 2010. Enrollment levels at the Texas dental schools are unlikely to change much over the remainder of the decade. Dental enrollments are limited by the size of facilities. Significant increases in dental school enrollments can only occur if new or expanded clinical facilities are developed.
In the spring of 1961, during my sophomore year of medical school at Johns Hopkins, I had an elective quarter at Guy’s Hospital in London along with my roommate, Larry Kirkland. Shortly before that, I had encountered an old friend of mine at Davidson College, Don Stewart (now a neurosurgeon), who explained that he had spent a wonderful year at London at St. Thomas Hospital (Figure 1).

Don suggested that in London I should immediately contact John Ormsby-Gore at the “St. Thomas Club.” I found that the St. Thomas Club was a club for medical students that had a bar and was across from the hospital, which was on Lambeth Palace Road and Southwark on the Thames River. After a few weeks in London, I decided to call John; it was fairly late, around 9:30 pm. He talked to me shortly on the phone, asked about my location, and immediately said, “I will send a taxi to you soon!”

About 30 minutes later, I found John at the St. Thomas Club enthraling several medical students with continual stories. John was also a medical student but seemed somewhat older, in his mid 30s. He was an excellent host, offering several beers (English “pints of bitter”). The time of midnight came shortly, and I was invited to go to an Indian restaurant with the group. They explained their custom: “We English never have dinner before midnight!”

About 30 minutes later, I found John at the St. Thomas Club enthraling several medical students with continual stories. John was also a medical student but seemed somewhat older, in his mid 30s. He was an excellent host, offering several beers (English “pints of bitter”). The time of midnight came shortly, and I was invited to go to an Indian restaurant with the group. They explained their custom: “We English never have dinner before midnight!”

I discovered that John Ormsby-Gore had been a medical student at St. Thomas for a long time—perhaps as long as 15 years—after serving in World War II as a military officer. John’s father was a “lord,” a former member of Parliament, and an authority on archeology. John’s brother was said to be the ambassador to the United States and a close friend of President John F. Kennedy. John had also met “JFK” but was not really in the “same circle” and called himself the “black sheep” of his family.

When I asked John about his medical school activities, he talked about spending almost every night at the St. Thomas Club and serving as manager of the St. Thomas rugby and cricket squads. He did not talk much about his experiences in his medical school courses and clinical work. When I asked about his plans for finishing medical school and the required “qualification tests,” he said: “Oh, I’ve considered the ‘qualifications,’ but it’s very tough and takes about 6 months’ work before the test, and every time I seem to think about the test, it’s at the same time as the Royal Ascot, to which I always go!” The Royal Ascot (Figure 2) is traditionally held during the third week in June and is England’s annual display of horse racing and hat pageantry. It is also closely associated with the British royal family.

John Ormsby-Gore was always hospitable to me during my several weeks in London. He was an encyclopedia of all the important events in London and also suggested the best travel places in England, Scotland, and Wales. I recalled a special Saturday in mid June with John showing me and Larry the “Trooping the Colours” annual parade (Figure 3) in London, in which the
queen’s personal troops honor her official birthday. This display of pageantry dates back to the time of Charles II in the 17th century. Not many tourists could find this unique event.

More than 40 years after my wonderful 10-week stay in London, I continued to try to find what had happened to John Ormsby-Gore. I contacted St. Thomas to find his address without success. Finally I decided to use the Internet and found very unusual facts about the Ormsby-Gore family.

John Ormsby-Gore (1816–1876) was the first Baron Harlech and was a British Conservative member of Parliament. He was elected to the House of Commons for Carnarvonshire in 1837. William Ormsby-Gore (1885–1964), the fourth Baron Harlech, was the father of our friend, John Ormsby-Gore. He was also a Conservative member of Parliament. David Ormsby-Gore (1918–1985) was the fifth Baron Harlech and a British diplomat and Conservative member of Parliament from Oswestry in Shropshire. He was John’s older brother and had been educated at Eton College and Oxford University. David knew John F. Kennedy well from Kennedy’s time in London while his father, Joseph P. Kennedy, had served as the American ambassador. After Kennedy’s election as president, David was appointed British ambassador to the United States from 1961 to 1965. In 1965 he took his seat in the House of Lords as Lord Harlech. He also had a successful career as a television executive.

The family later had several tragedies. Of David’s five children, one son died of gunshot wounds, an apparent suicide, and one daughter was engaged to rock guitarist Eric Clapton in 1969 and later died of a heroin overdose. (Another daughter had an affair with Mick Jagger during the 1960s.) Lady Harlech died in a car accident in 1967, and Lord Harlech died in a car crash near his home in 1985.

David was succeeded in the barony by his second son, Francis Ormsby-Gore, the sixth Baron Harlech. However, in 2011, this Lord Harlech and his daughter were involved in a dangerous driving incident in North Wales. He had lived in Brogyntyn Hall near Oswestry in Shropshire, England, close to the Welch border.

In the past few years I have read of several Ormsby-Gore family celebrities and also tragedies and accidents. Despite this, I was able to find very little about my good friend John Ormsby-Gore. Internet sources provided only four lines about him recently:

Capt. The Hon. John Julian Stafford Ormsby-Gore, late of the Coldstream Guards, and educated from Eton College and Oxford University, who died in 18 April, 2008, after a short illness, age 83, a son of the 4th Baron Harlech.

Unfortunately, there was no information concerning his medical experience at St. Thomas Medical School, although he was cited as a “British nobility.”

My roommate, Dr. Larry Kirkland, and I still remember our kind, hospitable English medical friends. We especially remember Dr. Dick Squires, who was also in medical school at St. Thomas and invited us to spend a weekend with him in his home in Wantage, Oxfordshire, England, only a few feet away from the statue of King Alfred the Great (871–899) (Figure 4). I have had the fortune of visiting Dr. Dick Squires two other times and most recently saw his restored Lains Barn dating in part from 1750, which is now used for community and educational functions. Dick is now a member of the Order of the British Empire.
For the Love of Wild Places by Greg and Mary Beth Dimijian


Reviewed by Daniel E. Polter, MD

For the Love of Wild Places is a memoir of Greg and Mary Beth Dimijian’s travels to remote parts of our planet, relating an extensive knowledge of the wildlife, natural history, biology, geology, and ecology of the sites they visited. They documented their adventures with unique and artistic photographs of life in some of the most interesting places on earth.

Greg is an unusual personality. He is a modern-day polymath, a psychiatrist with special expertise in addiction, a self-taught biologist and ecologist, a photographer and artist with his camera, and a former pilot. As a teenager he considered a career as a concert pianist. This multitude of interests became wedded to a love of nature and adventure during a summer as a young park ranger in Glacier National Park.

Chapters cover life in tropical rainforests; African wildlife in the Serengeti and the Okavango Delta of Botswana; Antarctica and the magical South Georgia Island; active volcanoes in Costa Rica, Hawaii, and Iceland; the underwater world of coral reefs; and remote and beautiful places in America. This work contains many scientific tidbits, illustrating the tremendous complexity of nature. A typical example is the Leafcutter. Leafcutter ants in the tropics bring leaf fragments back to their nest, which provides food for a type of soil fungus. The fungus then secretes a substance that serves as food for the ants. This is termed mutualism. Another example of mutualism is the fig wasp-fig relationship. Most tropical figs are dependent on a tiny wasp for pollination. The wasp itself relies on the fig fruit for its own reproduction. The wasp burrows into the unripe fig, which interestingly is part flower and part fruit. The wasps depart before the fig ripens.

This book is a delightful treat for travelers who have visited some of the places described by the authors. For those who plan to travel to any of these sites it is a helpful introduction, and for those who enjoy learning about our natural world it is informative and entertaining. The photographs are stunning and the narrative is well written. It is a worthy homage to our beautiful and amazing planet.

The reviewer, Daniel E. Polter, MD, is a gastroenterologist on the medical staff of Baylor University Medical Center at Dallas.
As an academic medical scientist, I do not traditionally write reviews of poetry. However, in Dr. Khan’s poetry, I found his heart speaking to my heart. Such a conversation elicited a drive to share and urge others to experience the same energy.

Dr. Khan is a medical oncologist and scientist who is itching to apprehend the secrets of immortality being so well perfected by the cancer cells. For years I have been enjoying his association, along with that of his poetry composed in our mother tongue. Frankly, I did not expect a book from him written in the language we adopted in our new home country. That certainly proves that poetry is a language of the heart without recognizing any frontier.

There are a string of spiritual and reforming poets that we remember as enlightened souls of the Sufi tradition. Guru Nanak, Baba Farid, Baba Waris Shah, Mian Mir, and Baba Bulleh Shah, among them, lived in the more recent past. They were humanists, pluralists, and philosophers. Guru Nanak was the founder of the Sikh religion. Mian Mir laid the foundation stone of the Golden Temple Sikh Shrine. In Dr. Khan’s poetry, I sensed the Sufi wisdom and belief traditions that were for the first time expressed, and not just translated, by a scientist in the English language.

The first thing that strikes the reader of Dr. Khan’s book is its coverage of life aspects that are diverse and vast. The book consists of 80 poems divided into six chapters and an introduction. He starts the book with “Let me paint my roses; Let me share my thorns” and ends with “Let me chase infinity. Let the ideas soar.” Those statements say a lot about the wide coverage he undertakes.

He begins with a poem on River Ravi, which divides the Punjab State of India and the Punjab State of Pakistan. The only bridge on the river connecting the two states was built by the British and was destroyed by bombs in the wars between India and Pakistan. The banks of this river witnessed a rich history of prophets who were born and lived on its banks and the sad history of political upheavals and fights. Presently this river separates the sacred shrine of Guru Nanak from his followers. Here Guru Nanak spent the last 18 years of his life establishing the Sikh religion. His followers, now in the millions, live on the other side of the river bank and come twice a day to gaze at their sacred shrine for prayer from a distance. Dr. Khan rightfully describes Ravi River as the “book of time.”

Then Dr. Khan goes on to grab the human soul: “The issue of the soul have many pondered, But the trail turned up cold.” Longevity to Dr. Khan is a “cruel bargain”: “Plum is bartered for a prune.” The readers will appreciate both the humor and the imagery.

Dr. Khan is disturbed over wars of religion—both wars of worship and wars among worshipers. He expressed his anguish in a poem on page 58: “A mosque on the north, a church on the south, And tranquil path lay between the two. . . . Belief was nestled at a chosen place. Not on forehead but the altar of heart.” I am going to refrain from describing every poem. Readers must have the opportunity to take their own dip and let their listening heart meet Dr. Khan’s speaking heart.

We live in a multifaceted environment, which asks for easily understandable imagery. In his poems, Dr. Khan has succeeded in simplifying complex issues of life in a way that a lay person may appreciate. I recommend this book for professional audiences and the public alike. Every reader will find *Sifting Shades* an engaging experience.
Cardiac rehabilitation in firefighters

We read the case series, “High-intensity, occupation-specific training in a series of firefighters during Phase II cardiac rehabilitation” by Adams et al (1) with great interest. We applaud the authors’ efforts to bring greater attention to the cardiovascular hazards of firefighting. However, we are extremely concerned that this article’s anecdotal report on six firefighters with a history of coronary revascularization provides physicians with the false impression that most firefighters should return to unrestricted fire department emergency duties after acute myocardial infarction, angioplasty, or cardiac surgery if they completed a similar cardiac rehabilitation program. Furthermore, the report fails to provide clinicians with the most relevant epidemiologic data regarding the risk of sudden cardiac death (SCD) during fire suppression and other fire emergency duties that would assist them to make more informed and evidence-based decisions on return to work in this dangerous occupation.

While the authors correctly note that SCD due to coronary heart disease (CHD) is the leading cause of death in U.S. firefighters (2), they do not mention key facts that drive this observation. First, firefighters with an established diagnosis of CHD (like the six patients reported on here) unnecessarily account for 25% to 30% of all on-duty CHD events and SCD (3, 4). Second, not only is a recurrent on-duty CHD event more likely, but the odds of case fatality during a firefighting CHD event are four times higher for those with a prior diagnosis of CHD after adjustment for other risk factors (5). The relative risk of on-duty SCD death for such individuals is 35 times that of their colleagues without a CHD history. In fact, even after accounting for all other comorbid cardiovascular disease risk factors, the relative risk of on-duty SCD remains about 15-fold higher (4). Clinicians almost never face risks of such magnitude and then decide that it is still acceptable for the individual to engage in such a strenuous occupational activity.

There are other major problems with this report. The authors fail to state how the patients were selected or medically cleared to participate in this program and do not mention or do not have any inclusion/exclusion criteria based on disease severity. At what point would they determine that a firefighter is not safe to enter the program? To the authors’ credit, they mention the CHD return to work criteria developed by the National Fire Protection Agency (NFPA) (6). From the data presented, however, the participants did not meet these criteria because of their persistent cardiovascular disease risk factors. Moreover, the authors do not describe how and when they determined that a cardiac rehabilitation program participant was eligible to return to work.

The authors mention that the NFPA standard recommends >12 METS aerobic capacity for safe return to firefighting activities, and the authors’ own previous paper on this subject showed that healthy firefighters required an average of 12 METS and >85% of their age-predicted max heart rate to complete a fire obstacle course (7). Clearly then, a safe cardiac rehabilitation program would need to address those aerobic capacity criteria as one of the many necessary requirements for determining safety to return to work. However, the rehabilitation subjects have no peak METS reported after completing the program. In addition, the peak heart rates during the cardiac rehabilitation program were uniformly below 150 bpm (and below 85% age-predicted heart rate max in 5/7 cases). This strongly suggests that even though they mimicked fire suppression activities in terms of muscular activities, the self-paced nature of the program allowed the participants to perform below the 12 MET threshold.

Published studies of various firefighter activities and conditions consistently demonstrate peak heart rates of >160–180 (8–11). Therefore, the intensity of a cardiac rehabilitation program targeting firefighters would need to be higher than the one reported by Adams et al to meet this demand. While beta blockade is offered as a reason for the low peak heart rates during exertion, such a confounding factor would make it even more imperative to objectively demonstrate participants’ aerobic capacities in a quantitative fashion. Accordingly, while the cardiac rehabilitation program the authors present is unique, it by no means simulates or approximates the cardiovascular stressors of actual fire suppression duties for all of the reasons above. To the authors’ credit, they acknowledge that the program has no element of shift work, heat stress, dehydration, low oxygen tension, or exposure to inhalational toxins, which are additional cardiac stressors and part of the essential job duties that the returning cardiac patient would face (12, 13). Again, however, they fail to explain how they would infer from such limited data in a safe and controlled environment the participants’ ability to safely return to work under complex, unpredictable, and dangerous conditions.

An even more serious flaw of the paper is that the methodology cannot support any of the claims made by the authors about their proposed cardiac rehabilitation regimen. There is no presentation of pre- and post-rehabilitation exercise data (e.g., peak exercise heart rate and blood pressure response, electrocardiographic patterns during exertion, or aerobic capacity) to show that the firefighters were more fit and had better cardiovascular responses to exertion after completing the program. Firefighters did not complete a standard fire service Physical Abilities Test and did not (or it was not reported) achieve 12 METS as a more standardized surrogate measure of the ability to safely perform essential firefighting duties. Finally, no longitudinal follow-up was provided to document that the patients had indeed “safely” returned to unrestricted duties without further incidents. Thus, while we agree that
The authors respond:

We appreciate the opportunity to respond to the letter by Kales et al regarding our article published in *BUMC Proceedings* (1). We would like first to emphasize that the high-intensity, occupation-specific training (HIOST) program described in our case series was never meant to be used to clear firefighters for return to active duty. The National Fire Protection Association’s own guidelines (2) recommend a single exercise stress test to help physicians decide whether firefighters with coronary heart disease (CHD) can return to work. In our opinion, this is inadequate. Our HIOST cardiac rehabilitation program is intended to make available more detailed information than a single exercise stress test may provide.

Kales et al explain the facts that drive CHD as the leading cause of sudden cardiac death (SCD) in US firefighters. The authors’ previous report (3) is cited as evidence of increased risk of SCD in firefighters with prior CHD. However, the study grouped patients together and labeled them with a diagnosis of previous CHD if they had any of the following: a previous abnormal exercise or radionuclide stress test or a history of coronary artery bypass grafting, coronary angioplasty, myocardial infarction, angina pectoris, carotid stenosis, or peripheral arterial disease. This is an extremely varied patient population. Our point is that the individual firefighter, not a single diagnosis, should be considered when determining whether the patient should be allowed to return to work.

Kales et al correctly point out that there is a selection bias in our case series, as firefighters themselves determined if they wanted to participate. We readily acknowledge that not all firefighters would be able to participate in HIOST following coronary revascularization events. However, as reported by the authors previously, many firefighters have uncontrolled cardiovascular risk factors (3) and have undiagnosed CHD. It is noted that 75% of firefighters with CHD-related deaths had no recent fire department medical examination (3). We are concerned that many firefighters may not seek medical attention and cardiovascular risk stratification because receiving a diagnosis of CHD may not allow a return to work. We also believe that the availability of structured post–coronary revascularization programs like HIOST in a cardiac rehabilitation setting will encourage firefighters to seek cardiovascular risk stratification.

Kales et al also are concerned that we have not reported whether participants were eligible to return to work and that no longitudinal follow-up was provided. Tracking return to work in this patient population can be misleading. There are many confounding factors that may be used in the final decision about return to work that have nothing to do with the exercise training in cardiac rehabilitation. Examples include workplace and/or physician denial, spouse refusal, fear, department policies, and current existing guidelines.

Kales et al cite concerns that our report has not simulated sufficiently the aerobic capacity requirements of firefighting activities (4). We would again acknowledge that beta-blockade therapy likely explains the blunted heart rates. In addition, the activities completed by the firefighters in our report mirrored the 12-MET activities from our prior study (4).

To reiterate, we did not intend for the information in this report to be used for clearing individuals to return to active firefighting.
duties. We believe this is an individual decision that should be made with as much clinical information as possible and not solely because of the presence or absence of a particular diagnosis. Limited data exist on firefighters’ ability to perform firefighting tasks following successful coronary revascularization procedures. We hope that ours is the first of many reports to explore firefighter safety following coronary revascularization.

—Rafic Berbarie, MD, Jenny Adams, PhD, and Tim Bilbrey, BS
Cardiac Rehabilitation Department, Baylor Jack and Jane Hamilton Heart and Vascular Hospital, Dallas, Texas

ALTERNATIVE MEDICINE

That includes everything from herbal supplements to crystal healing and acupuncture. About 50% of Americans use alternative medicine and 10% use it on their children, according to Paul Offit, the author of Do You Believe in Magic? The Sense and Nonsense of Alternative Medicine (1). Consumers of alternative medicine range from healthy people who pop the occasional supplement, hoping to ward off a cold, for example, to the seriously ill, who turn over their life savings to gurus promising miracles. Offit indicates that alternative medicine is a $34 billion a year industry whose key players are adept at using lawsuits, lobbyists, and legislation to protect their market. More than 54,000 varieties of supplements are on the market. There is a Congressional Dietary Supplement Caucus of legislators who look favorably on the industry. One congressman indicated that the alternative medicine industry is as tough as any industry lobbying in Washington. They want as little legislation as possible.

Alternative medicine proponents say it is popular because people want more control over their health. While some supplements are just high-priced placebos, others carry serious risks. Dietary supplements can be prescription medications in disguise. The most common offenders tend to be the “natural” supplements claiming to melt fat, build muscles, or boost sexual performance. The Food and Drug Administration (FDA) has found that hundreds of brands actually contain real drugs, including anabolic steroids and the active ingredient in Viagra. In April 2013, the FDA indicated that it had received 86 reports of illness and death due to body-building supplements that illegally contained a stimulant called DMAA, which is especially risky when combined with caffeine because it can raise the blood pressure with its consequences. The FDA in 2012 estimated that supplements cause 50,000 adverse reactions a year.

Some patients with serious illnesses delay proper therapy as they opt for alternative medicine. Apple founder Steve Jobs’ faith in alternative medicine may have cost him his life. Jobs was diagnosed with pancreatic cancer in 2003, and although revered for his brilliant mind, chose to delay surgery for 9 months in favor of acupuncture, herbs, and special diets. Jobs eventually had surgery and, later, a liver transplant, but it was too late. He died in 2011, 8 years after diagnosis. According to his physician he had the only kind of pancreatic cancer that is treatable and curable.

According to Offit, consumers are often taken in by the outrageous claims of the supplement producers or because they fall victim to hucksters’ charismatic personalities.

Many Americans also are unaware that supplements, unlike drugs, do not need to be approved by the FDA or tested for safety before going on the market! During all these years the FDA has banned only one supplement, namely Ephedra, which was taken off the market in 2004 after it was found to increase the risk of heart problems and death. The FDA’s authority with supplements is mostly “reactive.” The agency must wait for people to get hurt or die before it can remove an unsafe supplement from the market.

Beware of supplements!

MEDICAL SPAS

A piece by Melinda Beck indicates that states are tightening regulations on medical spas and wading into some disputes over where beauty treatments stop and the practice of medicine starts (2). Medical spas are fast-growing hybrids between day spas and doctors’ offices. They typically offer Botox injections, facial peels, laser skin treatments, and other minimally invasive cosmetic procedures. Some even add breast implants, tummy tucks, and chin, face, brow, and eyelid lifts. The International Spa Association now counts 1750 medical spas across the US, up from 471 in 2003. Some of the growth comes from dermatologists and plastic surgeons adding such services and amenities to their practices. But physicians trained in unrelated specialties, such as obstetrics or orthopedics, also are supplementing their incomes with the lucrative procedures that rarely are covered by insurance. Most of the services are performed by nonphysicians.

State regulations vary widely. Only a few require medical spas to be licensed. In some states, procedures from laser hair removal to liposuction can be performed by nonphysicians. Most require physician oversight, though the physician does not necessarily have to be on site or even in the same state.
Some serious injuries have prompted crackdowns. Florida now requires that liposuctions removing >2 pounds of fat be performed in a state-licensed surgical center with emergency equipment on hand. A new state law in Maryland requires the state health department to oversee cosmetic surgery facilities. Pennsylvania is presently weighing tighter rules on who can provide laser treatments. Some of the push for more regulation is being driven by dermatologists who say allowing nonphysicians to perform cosmetic procedures puts physicians at risk. Only a few states require medical spas to report injuries.

Laws requiring physicians to perform procedures do not guarantee confidence either. Several groups have sprung up to teach cosmetic procedures to physicians from other fields. The National Society of Cosmetic Physicians, for example, advertises 2-day workshops on laser liposuction, breast augmentation, and tummy tucks. The proposed medical spa law in New York would require physicians advertising themselves as “board certified” to specify which board. This kind of medical business is obviously quite profitable to those who do it.

THE REAL CHOLESTEROL-LOWERING MAGIC BULLET

My friend, cardiologist Robert L. Rosenthal, sent me a New York Times piece entitled “Rare mutation ignites race for cholesterol drug” (3). The article by Gina Kolata describes the development and early testing of a monoclonal antibody, made in living cells, with the ability to lower the low-density lipoprotein (LDL) cholesterol (the bad one) to levels lower than they were at birth, to as low as 12 mg/dL. The story began about a decade ago when some French researchers published a note in Nature Genetics describing three generations of a family with extremely high LDL levels—up to 466—and a strong history of coronary heart disease. The researchers found that the family had a mutation in a gene called PCSK9, which slowed the body’s ability to rid itself of LDL. The mutated gene leads to the soaring cholesterol levels.

The French study gave Jonathan C. Cohen and Helen H. Hobbs of the University of Texas Southwestern Medical Center in Dallas an idea. If a mutation in PCSK9 could lead to high LDL levels, perhaps there were mutations that did the opposite, namely lead to very low levels of LDL and protect against atherosclerosis. Cohen and Hobbs found in a Dallas study that about 2.5% of blacks had a single mutated PCSK9 gene that no longer functioned, and about 3.2% of whites had a less powerful mutation that hampered the gene but did not destroy it. Because people have two copies of every gene, one inherited from each parent, those with the newly discovered mutation did not have two mutated genes, but instead had one fully functioning PCSK9 gene and one that was disabled. Blacks with the mutation ended up with LDL levels averaging 100 instead of the usual 138, a 28% reduction; whites with a less powerful mutation had LDL levels averaging 117, about 15% lower than average. The people with one disabled gene had lower than normal LDL levels for their entire lives. Hobbs and Cohen found that blacks aged 45 to 64 with a single mutated gene seemed almost immune to coronary heart disease during a 15-year follow-up, and whites, who had the less powerful mutation, had a 46% reduction in the incidence of coronary heart disease. These findings led them to search for a mother and father who each carried the single mutated gene. They found one such couple and tested their daughter who had the rare double inheritance. The daughter was a 32-year-old aerobics instructor living in a Dallas suburb with her two young children. She was healthy. Her LDL was 14, a level unheard of in healthy adults. This aerobics instructor was only 1 of 2 people thus far found on planet Earth with the rare gene mutation inherited from both parents; the other person, a young healthy Zimbabwean woman, had an LDL of 15.

The discovery of the mutation and the two women with their extremely low LDL levels has set off one of the greatest medical chases ever among three pharmaceutical companies, Amgen, Pfizer, and Sanofi, to test and win approval for a drug that mimics the effects of the mutation, drives LDL levels to new lows, and prevents coronary heart disease and other forms of atherosclerotic disease. All three companies now have drugs in clinical trials and report that the results so far are exciting. Each company’s drug is a biologic. The drugs will be injected, probably twice a month. This is great news on the horizon for our most frequent cardiovascular disease, namely atherosclerosis, and its most frequent form, coronary heart disease (heart attack).

EXERCISE AND WEIGHT LOSS

Through the years I have heard many people talk about their desire to lose weight. Many have commented that they needed to exercise more. Dwyer-Lindgren and colleagues (5) in a recent article provide evidence that, although exercise can provide many health benefits, weight loss is usually not one of them. US obesity levels have risen over the past decade despite an increase in physical activity. For every 1% increase in physical activity, obesity rates declined by only one tenth of a percent. The researchers concluded that exercise alone is not enough to lose much weight.
COWS, NUMBERS, DROUGHT, AND PRICES

Wholesale beef prices rose in 2013 (6). The meatpackers have been paying more for cows after droughts the past two summers in Texas, Oklahoma, and other big cattle-ranching states. The dry weather parched pastures and drove up feed costs, forcing many ranchers to cull their herds. The nation’s cattle herd shrunk by 2% at the end of 2012 from a year earlier to under 90 million cows, the lowest level since 1952. That means fewer beef carcasses are making it through the industries’ supply chain. In 2012, Americans spent $288 per person on beef, a 4.2% rise from $277 a year earlier, as retail prices rose. US beef sales in 2012 reached $91 billion, up from $86 billion in 2011. The sales of beef in the first half of 2013 fell 1.7% from a year earlier. In contrast, pork volumes rose 3% and chicken volumes were flat. As beef prices rise, less beef is consumed. Because most Americans devour bovine muscle, an increase in price may be the only way to really decrease its consumption. The same happened with cigarettes: as the price rose, the number of smokers declined. It continues to be true: we kill the cows and then the cows kill us.

E-CIGARETTES

These are the battery-powered devices that turn heated nicotine-laced liquid into vapor (7). The market for this type of cigarette presently is small but growing rapidly, in part because it is increasingly seen as less harmful than conventional cigarettes. E-cigarettes, unlike traditional smokes, currently are not federally regulated. The FDA warned consumers in 2009 that the new technology could pose its own health risks and stressed the need for more study. The agency has said it is planning regulations that would treat e-cigarettes as tobacco products, but has provided no details thus far. More than a dozen states have banned e-cigarette sales to minors, and others have outlawed their use in enclosed public spaces.

The long-term impact of inhaling e-cigarette vapor, which contains other substances such as propylene glycol, has yet to be determined. But, could e-cigarettes, which currently offer flavors such as chocolate, strawberry, and pina colada, serve as a gateway to traditional cigarettes for young people? What kind of age restrictions and warnings should e-cigarettes carry? What about advertising? E-cigarette sellers are not currently allowed to make health or smoking cessation claims. Nevertheless, the potential market for e-cigarettes is huge. Industry experts say US retail sales of e-cigarettes could reach $1 billion in 2013, just 1% of the country’s cigarette market but twice that of 2012. It’s better not to use a-, b-, c-, d-, or e-cigarettes!

CARE GIVING FOR THE ELDERLY

Kelly Greene (8) discussed the problem of overseeing home health care for elderly patients. In 2011 alone, the most recent data available, so-called informal caregivers provided at least 11.2 billion hours of unpaid care to family members and friends. That commitment is expected to escalate. In 2010, about 4% of adults under age 65 were providing unpaid care to relatives or friends who were 65 and older. By 2050, demand for informal caregivers could double to 8% as the younger population shrinks relative to the elderly population. Elderly people and their families also spent at least $3 billion on their own in 2011 on long-term care in the community, mainly at home, in addition to $36 billion on nursing homes and other long-term care facilities. And those figures do not necessarily include drugs not covered by Medicare and other unreimbursed expenses, such as food for special diets, increased utility costs, home renovations, and special supplies. One third of adults 65 or older and two thirds of those who have reached their mid 80s have functional limitations, needing help with tasks ranging from eating and bathing to preparing meals or paying bills. Four out of five older adults who fit that description still are living in the community rather than in a nursing home.

Greene provided suggestions for helping families cope with paying for more care at the same time they are stretched by the unpaid time they are spending providing it themselves:

1. Hire your own homecare professional or become one yourself.
2. Take the tax breaks. Many elder-care expenses qualify for a medical expense deduction from federal income taxes. It is still 7.5% for people 65 and older. If you hire paid caregivers on your own, rather than working through an agency, the parent has to report the caregivers’ income, either on a W-2 or 1099 form, to be able to deduct the expense. The adult child can take deductions only if the parent is a dependent and the child pays. Home improvements made with a physician’s prescription are tax deductible also. Such remodeling could include adding an elevator, swimming pool, central air conditioning, or ramps. The key is getting the physician’s note and deducting only the amount “over and above the amount it increases the home’s value.” One other possible medical expense deduction is entrance fees to a continuing-care retirement community, which provides care ranging from independent living to skilled nursing. The fees can run to >$100,000.
3. Designate a bookkeeper. People planning for later life should decide who should handle their finances in a health crisis, including designating who in the family should take control of the parents’ finances when needed, taking inventory of the parents’ resources, making sure the parents’ will and power of attorney are current, and pinpointing resources to pay for care costs.
4. Remember the veterans. The “aid and attendance” benefit of wartime veterans pays up to $2054 a month to married veterans who qualify. Single veterans and surviving spouses can qualify for smaller amounts. To qualify, veterans generally must have served at least 90 days of active military service, including at least one day during a war. The income limits are met after deducting unreimbursed medical expenses, including any long-term care expenses.
5. Embrace respite care. Respite care is short-term care designed to give the regular caregiver a break. One person who cared for her mother sometimes would take her mother to a hospital facility for a week for what was called respite care. These respite programs are available nationwide through...
social service agencies, nonprofit groups, and long-term care providers (eldercare.gov).

6. Know when to consider a permanent facility. Home care works best if you need a visiting nurse 3 or 4 times a week. But dementia requires round-the-clock care, and in these circumstances a nursing home or assisted living facility can be considerably less expensive.

As George Burns said, “Getting old is not for sissies.”

HOSPITAL CACOPHONY

Hospital noise is constant: the beeping of a heart monitor; the opening of doors by a nurse to take vital signs; changing shift conversations; overhead pagers; a visitor’s cell phone conversation; television; rattling dishes in a moving cart; an alarm going off when an intravenous medication is finished (9). Noise reduction efforts began gaining momentum in 2012 when Medicare began basing a portion of hospital reimbursement on quality measurements, including patient ratings of the quality of care. (Noise consistently gets the worst marks on patient surveys!) The latest data from the federal program for the year ending June 2012 showed that only 60% of patients said the area outside their room was quiet at night, the lowest satisfaction score among 27 questions about the hospital experience.

Several hospital administrators have cited changing behavior and culture as the biggest challenge to reducing hospital noise. Many hospitals now have only private rooms. Noise remains harder to control in shared rooms. A complicating factor is hospitals’ increasing openness, including more liberal visiting hours and policies that permit cell phones and other devices. Some hospitals have formed “quiet teams” to identify ways to reduce noise. Some are reducing the frequency and intensity of medical alarms, dimming lights in the evenings, and replacing nurses’ pagers and walkie-talkies with mobile headsets. Patients are getting Quiet Kits, white-noise machines and headsets for TVs and iPads. Some hospitals have hired consultants offering “sound scrapping” solutions, including architectural changes and the use of ambient sound.

Some consultants apparently suggest that hospitals “stop chasing silence” and increase the ratio of good sounds to bad sounds. Complete silence can actually be worrisome and isolating. The sickest patients may want quality sleep, but they also want to feel connected to their caregivers and know that they are not far away in case of an emergency. Some hospitals are asking staffers to use “library” voices because quiet murmurs can be more comforting than normal speaking tones. A recent study at Baylor Health Care System’s Heart Hospital in Plano found that white-noise machines made no difference in patients’ perception of noises in rooms. Terri Nuss has indicated that smooth hard surfaces enhance noise but they are easy to clean and help fight infection. Ms. Nuss indicates that Baylor University Medical Center at Dallas is trying to figure out what is an acceptable sound level. We can all be a little quieter.

END-OF-LIFE PREFERENCES

Ellen Goodman, a favorite of mine, retired as a widely syndicated columnist about a year ago and founded the Conversation Project (theconversationproject.org), a national campaign to encourage conversations about our wishes for end-of-life care (10). Dying is not easy today. Too often, of course, feeding tubes and life support abound. A fractious family may play out its contentious relationships. Every day in this country, Ellen Goodman opines, thousands of families face these crises without being able to call on the voice of the person they love. It is a familiar drama in an era when death is no longer likely to be natural. How do we know when medical technology extends life and when it prolongs suffering? Goodman indicates that the thousands of people who have used the Conversation Starter Kit on the website state that with help these talks can be far more intimate than intimidating. Goodman indicates that since she launched the project it seems as if everyone has a story to tell of a good death or a hard death. The difference often hinged on whether people they loved had expressed their wishes and, in turn, had those wishes respected. It is clear that too many people are dying in a way they would not choose. Surveys indicate that 70% of Americans want to die at home, yet 70% end up dying in hospitals and institutions. At home, one is at least surrounded by loved ones in comfort and in peace. Too many survivors are left not just mourning but feeling guilty, depressed, and uncertain of whether they have done the right thing—done what their mother, father, husband, friend would have wanted, if he or she had said. Have you had the conversation?

GUIDELINES ON FOOD IMPORTED TO THE US

In July 2013, the FDA proposed new steps to ensure that fresh produce, cheeses, and other foods imported to the US are safe (11). The proposed rules, required by a sweeping Food Safety Law passed by Congress 2 years ago, are meant to establish better checks on what has long been a scattershot effort to guard against unsafe food imported from >150 countries. Only around 2% of that food is inspected by the US government at ports and borders. About 15% of the food Americans eat is imported, including about 50% of fruits and 20% of vegetables. An estimated 3000 people die from food-related illnesses in the US every year.

The proposed guidelines require US food importers to verify that the foreign companies they are importing from are achieving the same levels of food safety required in the USA. The rules, which would also improve audits of food facilities abroad, could cost the food industry up to $470 million annually.

Since Congress passed the Food Safety Law in December 2010, several outbreaks have been caused by imported foods, including an occurrence of Listeria in imported Italian cheese in 2012 that killed 4 people. Other illnesses were linked to tainted papayas, mangoes, and nuts and spices used as ingredients. Like rules for domestic farmers and food companies released in early 2013, the idea of the new guidelines is to make businesses more responsible for the food they sell or import by proving that they are using good food safety practices. Currently, the government does little to ensure that companies are trying to prevent food safety problems rather than waiting and responding to outbreaks after they happen. Requiring better prevention was the intent when Congress passed the bill. Since then, however, the law
has run into several obstacles, including FDA delays in issuing the guidelines, a lack of congressional funding, and increasing opposition from some rural members of Congress who represent worried farmers. FDA regulators say the new rules are necessary as the food system becomes more complex and more global. Food often stops in several locations and passes through several different hands in a matter of days before it hits grocery shelves. A lack of funding also has given the FDA little oversight over what is produced. The agency inspects most food companies in the US only once every 5 to 10 years, and it does even fewer inspections abroad. The Food Safety Law requires the agency to step up those inspections. In 2012, the FDA inspected about 1300 facilities in foreign countries, up from 300 in 2010. That is still just a fraction of the companies that import to the USA. Sounds reasonable.

DESTROYING CHINA’S EARTH

Josh Chin and Brian Spegele (12) recently described some experiences of farmers in central China’s Hunan province. They highlight an emerging and critical front in China’s intensifying battle with pollution. For years, the focus was on the choking air and contaminated water that plagued China’s ever-expanding cities. A series of recent events, however, has highlighted the spread of pollution outside of urban areas, now encompassing vast swaths of countryside, including the agricultural heartland. Estimates from state-affiliated researchers indicate that anywhere from 10% to 20% of arable land, some 25 to 60 million acres, may be contaminated with heavy metals. A loss of even 5% could be disastrous, taking China below the “red line” of 296 million acres of arable land currently needed, according to its government, to feed the country’s 1.35 billion people.

Rural China’s toxic turn is largely a consequence of two trends: the expansion of polluting industries into remote areas and the heavy use of chemical fertilizers to meet the country’s mounting food needs. Both changes have been driven by the rapid pace of urbanization in a country that in 2012 for the first time had more people living in cities than outside of them. Yet, the effort to keep urbanites comfortable and well fed has also led to the poisoning of parts of the food chain, and some of that pollution is traveling back to the cities in a different guise. Judith Shapiro, the US-based author of the recent book China’s Environmental Challenges, indicates that pollution can be displaced only to an extent and that it cannot be walled off. She among others has warned that pollution poses an existential threat to the current regime. Shapiro says that the single most significant determinant of whether the Communist Party will maintain its legitimacy in coming years will be its ability to control that pollution.

China has sought to industrialize its countryside for the last 50 years when it began urging peasants to set up backyard steel furnaces at the expense of agricultural output. The cumulative impact of decades of building up rural industry is now taking an environmental toll, particularly as industrial growth surges forward in China’s breadbasket. In some cases, factories are moving to the countryside to take advantage of cheaper land, often made available with the help of local officials who want to boost growth. In other cases, urban leaders want factories to move out of crowded cities. The ensuing problems of rural pollution are exacerbated by the fact that many small-town governments have less capacity to properly regulate complex industrial activities than their counterparts in big cities. The consequences of this shift catapulted to national attention in February 2013 when China’s Ministry of Environmental Protection refused to release the results of a multiyear nationwide soil-pollution survey, calling the data a “state secret.” The decision sparked an outcry. Many farmers who farmed lands adjacent to various factories now cannot eat what they grow but by still farming the land they receive payments from the factory owners to compensate for polluting the ground. Bad deal!

US MEDICAL COSTS

As nearly everyone knows, Americans pay more for almost every interaction with the medical system than do people residing in other developed nations (15). They are typically prescribed more expensive procedures and tests than people in other countries, regardless of whether those nations operate a private or national health system. A list of drug, scan, and procedure prices compiled by the International Federation of Health Plans, a global network of health insurers, found that the US came out the most costly in all 21 categories and often by a huge margin. Americans pay, on average, about 4 times as much for a hip replacement as patients in Switzerland or France and 3 times as much for a Cesarean section as those in New Zealand or the UK. The costs of hospital stays in the US are about triple those in other developed countries, even though they last no longer. While the US medical system is famous for use of drugs costing hundreds of thousands of dollars and heroic care at the end of life, a much more significant factor in the nation’s $2.7 trillion annual health care bill is not the use of extraordinary services but the high price tag of ordinary ones. The US pays providers of health care much more for everything. Colonoscopies are the most expensive screening test that healthy Americans routinely undergo. They often cost more than childbirth or appendectomy in most other developed countries. Their numbers have increased many fold over the last 15 years, and data from the Centers for Disease Control and Prevention suggest that more than 10 million people get them each year, adding up to more than $10 billion in annual costs. Largely an office procedure when widespread screening was first recommended, colonoscopies have moved into surgery centers where they are billed like a quasi-operation.

As Elisabeth Rosenthal writes, “Hospitals, drug companies, device makers, physicians, and other providers can benefit by charging inflated prices, favoring the most costly treatment options, and curbing competition that could give patients more and cheaper choices. And almost every interaction can be an opportunity to send multiple, often opaque bills with long lists of charges.”

The United States spends about 18% of its gross domestic product (GDP) on health care—nearly twice as much as most other developed countries. While the rise in health care spending in the US has slowed in the past 4 years—to about 4%
annually from about 8%—it is still expected to rise faster than the GDP. Aging baby boomers and tens of millions of patients newly insured under the Affordable Care Act are likely to add to the burden.

Consumers of medical care, the patients, do not see prices until after a service is provided, if they see them at all. Patients with insurance pay a tiny fraction of the bill, providing scant disincentive for spending. Physicians often do not know the cost of the tests and procedures they order. Without posted prices, how can one make an intelligent decision? This situation is unique to medicine, where payments are often determined in countless negotiations between a physician, hospital or pharmacy, and an insurer, with the result often depending on their relative negotiating power. Insurers have limited incentive to bargain forcefully since they can raise premiums to cover costs. How medicine got into this situation is a bit unclear to me, and determining a reasonable solution will be a challenge for all.

TEXAS DEBT

According to Steven Malanga (14), Texas’ combined state and local debt as of 2011 is just over $233 billion! While state government debt stands at $40 billion, or $1577 per resident, local government debt is >4 times as high: $192 billion, or $7505 per person, the second highest sum in the nation behind only New York’s municipalities and far ahead of third place California. During the last 10 years local debt in Texas has increased 144%, much faster than the rate of population increase plus inflation.

Where is all this debt coming from? One place is the huge expenditures by local school districts on athletic facilities. Allen, for example, just spent $60 million on its new high school stadium, and its population is only 83,000. The 18,000-seat facility, which boasts a massive high-definition TV screen, was built from funds generated by a $119 million bond offering. More than 100 new high school stadiums have opened in Texas during the last 5 years, and that does not include pricey upgrades in several.

Debt owed by public school districts constitutes the biggest chunk of the state’s soaring local obligations. Over the last decade, it has increased 155%, even as the state’s student population has grown just 21%. Interest payments on these school debts now constitute 10% of school spending ($5.5 billion).

Debt is also growing rapidly among the state’s 81 retirement systems for local government workers. These systems are underfunded. A result of this underfunding means that the contributions to pension systems that municipalities must make each year are rising, eating up large portions of local budgets. Additionally, employee costs are rising locally, going from 15% of city budgets to 30%. Those cost increases are partly to blame for sharp increases in property taxes: 38% in the last decade, it has increased 155%, even as the state’s student population is only 83,000. The 18,000-seat facility, which boasts a massive high-definition TV screen, was built from funds generated by a $119 million bond offering. More than 100 new high school stadiums have opened in Texas during the last 5 years, and that does not include pricey upgrades in several.

Debt owed by public school districts constitutes the biggest chunk of the state’s soaring local obligations. Over the last decade, it has increased 155%, even as the state’s student population has grown just 21%. Interest payments on these school debts now constitute 10% of school spending ($5.5 billion).

Debt is also growing rapidly among the state’s 81 retirement systems for local government workers. These systems are underfunded. A result of this underfunding means that the contributions to pension systems that municipalities must make each year are rising, eating up large portions of local budgets. Additionally, employee costs are rising locally, going from 15% of city budgets to 30%. Those cost increases are partly to blame for sharp increases in property taxes: 38% in the last decade. I thought California, New York, and Illinois were the big debt states, but that seems not to be the entire story.

HIGHEST-PAID STATE EMPLOYEES

My friend, Robert Doroghazi of Columbia, Missouri, a retired cardiologist who writes a wonderful biweekly investor newsletter, *The Physician Investor Newsletter* (www.thephysicianinvestor.com), to which I have subscribed for several years, recently had a piece on the highest-paid state employees in the USA (15). They were as follows: football coach, 27; basketball coach, 11; football/basketball coach, 1; hockey coach, 1; college president, 4; medical school dean/administrator, 5; and law school dean, 1. Thus, our society, as Doroghazi comments, rewards sport coaches more than university presidents and medical school deans. Our society also rewards the average Major League Baseball players 5 times more than the average physician ($1.3 million vs. $241,000) (16).

TOP CITIES FOR JOBS

Between 2009 and the end of 2011, Texas added 428,000 jobs to restore the Lone Star State to its prerecession employment level, which it achieved faster than any other state (17). Of the top 10 US cities for jobs, four are in Texas, including Fort Worth, #4; Houston, #5; Dallas, #6; and Austin, #10. Since 2001, employment in Houston has expanded 20%; in Fort Worth, 16%; in Dallas, 11%; and in Austin, 27%. The oil and gas boom has been a big factor, particularly in Houston, but growth has also been strong in technology, manufacturing, and business services. Good for Texas!

STEM JOBS

They are jobs that require some knowledge of science, technology, engineering, or math. A June 2013 report from the Brookings Institution disclosed that the number of US jobs that now require STEM knowledge is 26 million as of 2011, or 20% of all jobs (18). In Dallas–Fort Worth, STEM jobs also make up 20% of all jobs. Pay and employment rates are higher for all STEM workers compared to non-STEM workers. For all STEM jobs in the Dallas–Fort Worth area, the average pay is $70,000, whereas for non-STEM jobs, it is $40,000. For jobs requiring a bachelor’s degree or higher, the average STEM salary is $88,000 and the average non-STEM salary is $68,000. Study hard, young folks, particularly in science, technology, engineering, and math courses.

SMARTPHONE ADDICTION

In-Soo Nam (19) described smartphone addiction in high school students in South Korea. She defined this addiction as spending >7 hours a day using the phone and experiencing symptoms such as anxiety, insomnia, and depression when cut off from the device. She indicated that roughly 1 in 5 students in South Korea are addicted to the smartphone. In July 2013, the South Korean government said it plans to provide nationwide counseling programs for youngsters by the end of the year and train teachers on how to deal with students with addiction. Taxpayer-funded counseling treatments already exist in South Korea for adults addicted to smartphones.

South Korea, home of the world’s biggest smartphone maker, Samsung Electronics, prides itself on being the global leader in high-speed Internet and advanced mobile technology. Koreans are some of the first adopters of new digital devices. Their mobile phone penetration rate is more than 100%, meaning that some individuals carry more than one handset, and
smartphones are nearly two thirds of those devices. In contrast, the smartphone penetration rate in the US was 50% as of June 2013. (Korea also has had problems with online game addiction among teenagers for years thanks to widespread availability of high-speed Internet services.) The smartphone penetration rate in children aged 6 to 19 tripled to 65% in 2012 from a year earlier. The smartphone addiction rate among teens was 18%, double the addiction rate of 9% for adults. In the US in 2012, 37% of teens had smartphones.

The same problem appears to be surfacing also in other tech-savvy places such as Japan and Taiwan. According to experts, in addition to distracting students from their studies, smartphones are damaging their interpersonal skills. Students today, for example, are poor at reading facial expressions. One professor commented, “When you spend more time texting people instead of talking to them, you don’t learn how to read nonverbal language.” In Taiwan, the phenomenon of constantly checking e-mail or social media has led to the label “heads-down tribes.” The number of people in Taiwan accessing the Internet via laptops, tablets, or smartphones in the past 6 months has doubled to a record of 5.35 million from a year earlier.

It is now standard practice in Korean schools for teachers to collect mobile devices from their students during school hours. One teacher there commented that smartphones are often the most important possession for a young person.

POWER-GENERATING WIND TURBINES AND BIRDS

Wind turbines may exceed 400 feet in height, a space extending into bird flight paths (20). The spinning rotors can cover an area >1 acre. Birds scanning the ground for prey flying at night or gliding with the wind may fly directly into the path of a wind turbine, slamming into spinning blades, metal towers, or other structures. The blade tips can travel more than 150 miles per hour. A recent study estimates that approximately 575,000 birds, including species protected by federal law, are killed each year by collisions with power-generating wind turbines. That number could reach 1 million a year by 2030 as utilities install more wind farms. No matter what the power source, be it coal, oil, gas, water, or wind, there is suffering, be it from humans or salmon or birds or other species. There is really no such thing as “clean energy” despite what some of us might like to think.

BASEBALL DOWNTIME

My friend, Baylor surgeon G. Ken Hempel, recently took me and two others to a Texas Rangers baseball game. It was a wonderful evening. Ken picked me up at 5:15 pm, the game started at 7:05, and Ken dropped me back home about 11:00 pm. That nearly 6-hour period produced a great deal of relaxation and a few minutes of excitement. The Wall Street Journal recently had a piece on baseball downtime (21). During an average 3-hour Major League Baseball game, the inaction amounts to 2 hours 40 minutes, and the action about 20 minutes. The inaction provided much time to talk. During the game David Murphy hit a home run over the centerfield fence, which stands 425 feet from home plate. The question arose as to the longest home run ever hit. It was by Mickey Mantle, who hit one 634 feet—200 feet longer than David Murphy’s big blast and over two football fields in length.

In any given year, roughly 70 million people attend a Major League Baseball game. One thing every one of those fans sees is a bunch of grown men standing in a field doing absolutely nothing “about 90% of the time.” Baseball is known for its moments of action, but they are fleeting. Nevertheless, it is clear why this game is known as our “national pastime.”

TURNING NIGHT INTO DAY

Darkness was, for all of human existence, a universal obstacle to human happiness. In the late 19th century, the yearning for more light became more urgent. Many forms of work in the new industrial age, both in factories and offices, made more demands on the eyes, requiring greater attention to detail. At the same time, the urban world had grown darker, as tall buildings cast their shade and burning coal belched its smothering pall, blocking sunlight and coating windows with grime.

My father was born into this darkness when he entered the world in 1878; no city in the US was lit at that time. Although Thomas A. Edison had started working on the incandescent bulb in 1877, a year later there was still no reliable bulb. Although Edison made no claim that he had invented the first working light bulb, what he did create was a complete lighting system that linked his powerful and efficient dynamo, through a central main, to feeders and switches to his incandescent bulb of superior design. His system delivered a steady supply of current to hundreds of lights, at varying distances from the source of power, and used parallel circuits to maintain the current even when some of his lights burned out or were turned off. His bulbs used a filament of high resistance, a crucial innovation that saved money by using a relatively small amount of current for each lamp. In the 14-week light exposition in Paris in 1881, Edison showed that electric light not only worked but could be distributed some distance from a central station, a system with the potential to become large and economical enough to challenge the gas companies. Other inventors had shown that they could light a house, but Edison was on his way to lighting an entire city.

Ernest Freeberg recently published The Age of Edison: Electric Light and the Invention of Modern America, and what follows comes from his book (22). From the start, all recognized electric light as an agent of creative destruction that would only survive and thrive by stealing away gas customers. The gas companies were among the most heavily capitalized companies in the Western world. Right away, however, people saw that electric light was preferable to gas.

The first American showcase for street lighting (23 arc lamps) was a three-quarter mile stretch of Broadway in New York City installed by Charles Brush in 1880. Leaders in other cities sent delegations to see “the Great White Way” for themselves and to investigate the claims of the various lighting systems. Electric light’s first entrance into each new town was always a cause for civic celebration. The market for electric light grew rapidly in part because Americans embraced the idea that their town standing could be measured by its ability to provide residents with the latest technological conveniences. My hometown, Atlanta,
of the new lamps provided a steady glare, bright and mellow, and perhaps in the office or factory where they worked. But at a boulevard or park, in a department store, theater, or hotel lobby, most, however, experienced the new light on a daily basis. Dwellers in America lived with a new light on a daily basis.

In place of the usual dim flicker of gas, the bamboo filaments that were simplicity itself—a glass globe shaped like a dropping tear, enclosing a slender horseshoe of glowing carbon. There was no nauseous smell, no flicker, and little heat. Each light socket contained a key whereby the lamp may be turned on or off at pleasure. Oil lamps and candles in contrast required wick trimming and soot cleaning, while gas burners demanded even more technical skills from customers, who had to adjust meters and burners in addition to regular cleaning. The electric light required no maintenance while the source of power hummed out of sight, sometimes many city blocks away. The bulb worked for about 600 hours until it either broke or began to blacken and dim. Then an electric company worker could replace the expired bulb in a minute or two. The light bulb was safe enough for a child and simple enough for all to use. The functioning light bulb represented the culmination of decades of scientific insight, inventive genius, and technical skill.

While electric light made the urban night less dangerous, it also made it less private, exposing behavior that was not illegal but illicit. Everyone understood that in a world of crowded tenements, city parks provided a place not only for breathing but also for courting. By the middle of the 1880s, most town dwellers in America lived with a new light on a daily basis. Most, however, experienced the new light on the town’s main boulevard or park, in a department store, theater, or hotel lobby, and perhaps in the office or factory where they worked. But at the end of the evening, most returned to houses still lit by gas, kerosene, or oil lamps. Gas had not been driven from the field in the first decades of the electric light.

In the months following his 1881 triumph in Paris, Edison worked with his team to introduce improvements and efficiencies in every aspect of his invention, as he prepared to install his first central power station in downtown New York. He won permission to dig up the city streets and had the technical challenge of running 18 miles of copper mains and wires along with the fuses, meters, switches, and fixtures to serve >1000 customers. All of these elements were connected to his six 30-ton dynamos powered by coal housed in a 4-story building on a rundown block centrally located to reach downtown Manhattan customers for half a mile in every direction. By September 1882, Edison fired up thousands of lamps in a square mile of lower Manhattan. After years of painstaking preparation and a half million dollars of invested capital, the system turned on without a hitch. In place of the usual dim flicker of gas, the bamboo filaments of the new lamps provided a steady glare, bright and mellow, which illuminated interiors and showed through windows. The Edison bulb would become so ubiquitous, so mundane, that it would become invisible. Those using the first ones marveled that they were simplicity itself—a glass globe shaped like a dropping tear, enclosing a slender horseshoe of glowing carbon. There was no nauseous smell, no flicker, and little heat. Each light socket contained a key whereby the lamp may be turned on or off at pleasure. Oil lamps and candles in contrast required wick trimming and soot cleaning, while gas burners demanded even more technical skills from customers, who had to adjust meters and burners in addition to regular cleaning. The electric light required no maintenance while the source of power hummed out of sight, sometimes many city blocks away. The bulb worked for about 600 hours until it either broke or began to blacken and dim. Then an electric company worker could replace the expired bulb in a minute or two. The light bulb was safe enough for a child and simple enough for all to use. The functioning light bulb represented the culmination of decades of scientific insight, inventive genius, and technical skill.

Both Edison and his rival electricians sold standalone systems, single dynamos that fired a string of lamps, enough for a large house, store, or ship. But after the successful test of his Pearl Street station, Edison hoped to move forward with his much grander vision for an electrical grid, installing his central system in the urban core of every major city. Each territory offered a potential market of tens of thousands of lamps for office buildings, theaters, and the private residences of the elite. Edison’s company planned to sell its equipment to a local utility which would pay royalties and assume responsibility for finding and serving its customers. Once free from the obligation to oversee the daily operation of his New York power station, Edison devoted his time and resources to improving every aspect of his system. He founded a series of interlocking companies. He supervised their work in developing and manufacturing dynamos, underground conduits, fixtures, and bulbs. Edison set out to apply this strategy not only to the US, but around the world. He arranged similar partnerships with local utility operators in major cities in Europe, Asia, Central and South America, and Australia.

As the popularity of electric lights grew, the electric companies strung numerous high-tension wires along streets already thick with wires for telephones, telegraphs, fire and police alarms, and stock tickers. At dense urban intersections a pole might carry as many as 200 different wires. Those wires were unsightly. Initially, those wires used only a moderate current that posed no danger. All that changed when electric companies added their powerful and fully insulated high pressure arc wires to the mix. These often broke loose and fell across the web of other overhead wires. Traffic stopped and crowds gathered as wires burned and sparked. Once in contact with broken or sagging arc wires, harmless telegraph, fire alarm, and telephone wires delivered awful, even deadly shocks. At other times, they burned and melted, causing numerous fires. The firemen who came to the rescue faced not only the risk of the blaze but also the danger of electrocution.

For late 19th-century city dwellers, the sky overhead became increasingly ominous, thick with wires that might pour down a lightning bolt without warning. One medical journal declared that “the overhead system is a standing menace to life and health.” Every week the newspapers ran stories of this very modern form of sudden death. A Memphis man tied his mule to an iron lamp post that had been accidently electrified; the powerful current knocked the screaming mule off its feet and when its owner came to the rescue he leaned against the post himself and was instantly killed. Similar stories multiplied.

Most electric light victims worked for the companies, at a time when the properties of powerful currents were barely
understood and safety standards for the industry were just being invented. Many more were struck down while working around the dynamos, accidently completing a circuit that sent the powerful current through their bodies. At a time when prison reformers were exploring the use of electricity to execute prisoners, one editor suggested that death row inmates should simply be apprenticed to work for an electric light company because sooner or later the job would carry them off.

For all of human history, the rhythm of night and day exerted a powerful influence on how people arranged their lives. Nature seemed to intend the daylight hours for toil and the night for rest. This rough rule of thumb made sense in early America’s agricultural society but came under challenge during the 19th century’s illumination revolution. Although gas light and the new pressures of industrial production had already begun to blur the line between day and night, the more powerful electric light threatened to erase the distinction entirely. The electric light particularly complicated the primordial bifurcation by adding a third option—illuminating evening that mixed elements of brilliance and shadow, looking and feeling like nothing any human had experienced before. These lit hours between sundown and bedtime became a new piece of time. In many industries owners embraced electric lights’ economic potential, eager to keep their factories, mills, and shops open and their goods moving. Their workshops had required an enormous outlay of capital for expensive machinery and expanded facilities. To earn the best return on that investment, owners needed to keep those machines running as much as possible. As Henry Ford said some years later, “Expensive tools cannot remain idle. They ought to work 24 hours a day.” Thus, electricity would make possible the perpetual workday.

In the early days of the Industrial Revolution, workers relied on sunlight as their primary light source, often setting their benches as close as possible to the factories’ tall windows. The introduction of gas offered a stronger light for night work, but gas light was expensive, still caused fires and explosions, and, since it was not portable, proved useless in many work situations. Workers immediately noted the advantages of electric lights. The new light relieved them from the nasty smell and oppressive atmosphere of burning gas or oil lamps. In addition to having clearer heads, they enjoyed clear vision, no longer deceived by the flame’s yellow flicker. In some trades the more powerful light proved a useful tool of production, making work not only safer and faster, but also more accurate. Newspapers became early adopters of the new technology and often its greatest fans.

The transportation industry was another early adopter of the electric light, using it to extend the reach and value of the era’s powerful new railroads and steam ships, culminating by the early 20th century in a 24-hour per day distribution network. Lighthouses became popular.

Electricity was changing not only the way goods were produced but also how they were sold. Over time, merchants became sophisticated masters of light’s power to seduce customers. Stores installing electric lights were believed to have nothing to hide.

Physicians immediately recognized the potential value that the new light might provide to the healing arts, another field profoundly improved by its ability to illuminate a once invisible world. The electric light amplified the power and consistency of the microscope, which in turn helped to confirm the germ theory of disease. The conventional microscope had long revealed minuscule creatures in water and organic matter. The British scientist John Tyndall used a beam of electric light to demonstrate that the air itself carried an organic swarm of spores, bacteria, and other minute solid particles, a startling discovery that unsettled many but added support to Louis Pasteur’s germ theory. Electric lights powered to reveal this hidden world proved valuable to health officials as they tried to publicize these radical new ideas about the source and prevention of devastating urban scourges, such as cholera and typhus. Even as 19th-century science asked the public to accept its claims about a world beyond human senses, the new technology gave some of this a tangible reality. A drop of water presented the most extraordinary monsters imaginable, one reported after seeing one of these germ slides.

Surgeons embraced electric light technology almost immediately, another part of the late 19th-century revolutionary improvement in medical practice. Over the centuries, physicians had tried using candles and mirrors to reflect light into the body’s darkest corners and performed operations under skylights. Experts had recommended using the “cold north light” whenever possible since it cast less heat on the surgeon and fewer shadows on the patient. Physicians also had rigged devices to concentrate the beam of a candle or oil light, using it to illuminate translucent flesh and reveal the shadows casts by tumors and abscesses. The incandescent bulbs were cooler, flexible, and much brighter, and physicians used them almost immediately to provide the first clear look at the living tissues of the throat, nasal passages, urinary bladder, and other portions of the body. Within a few years, instrument makers had crafted a series of specialized surgical lights, each adapted for the unique challenges posed by the various surgical procedures. Physicians improved their power of diagnosis, sending the focused light of incandescent bulbs into every opening in the body. Dentists benefited as well, finding the light cool enough to use right against the teeth and gums, illuminating defects otherwise hidden beneath the surface. Along with the development of anesthetics and aseptic practices, electric light laid the foundation for modern surgery.

Still others explored the idea that the electric light itself might be good medicine. Patients with nervous diseases and depression were advised to replace their clear glass window panes with blue glass, and a Southern dentist swore by the use of an electric blue light for “the painless extraction of teeth.” Dr. John Harvey Kellogg pioneered the medical use of plain white electric light in his “laboratory of hygiene,” experimenting with the tonic effects of electric light. If the new urban environment disrupted sleep patterns and frayed nerves, producing a generation of Americans who retreated to sanitariums looking for a cure, then it was fortuitous for Kellogg to discover that the electric light, which had done so much to create these modern maladies, could also be
used to cure them. Kellogg thought that electric light was “nothing more nor less than a form of resuscitated sunshine.” Kellogg delivered light to thousands of patients, using what he called the “electric light bath.” The bather sat in a small cabinet, its interior lined with mirrors and studded with 60 incandescent bulbs. In this way patients dipped themselves into a healing “sea of light.” Kellogg claimed, “Shed upon the nude surface of the body the rays will enliven the nerves with renewed force and will dissipate and destroy the enumerable malefic influences which imperil health and life.” His electric light cabinet proved a good place to work up a sweat, stimulating the skin, accelerating respiration, and somehow encouraging the internal organs in their eliminative work. Saturating the body in the warm glow of incandescent light, Kellogg claimed, would prevent disease, heal skin conditions, nourish the body, and was the most agreeable means of reducing flesh, especially when the bather followed the electric bath with a brisk rubdown with salt or ice cold mittens.

And now the incandescent bulbs, in wide use since Thomas Edison received a patent for his version in 1880, are being phased out (23). A federal law passed in 2007 will end incandescent manufacturing and importing in the USA by the end of 2014, although stores will be allowed to keep them on the shelves until the inventory is gone. In their place will be the energy-efficient replacements (Halogen, CFL [compact fluorescent lamp], LED [light-emitting diode]), which are more expensive but last longer and require much less energy. Mr. Edison, thank you for the long and good run!

William Clifford Roberts, MD
12 August 2013

Selected published abstracts of Baylor researchers

**AMERICAN JOURNAL OF CARDIOLOGY**

Natural history of unoperated aortic stenosis during a 50-year period of cardiac valve replacement

Roberts WC, Vowels TJ, Filardo G, Ko JM, Mathur RP, Shirani J


Although a number of publications have described the natural history of patients with aortic stenosis (AS), the definition of “natural history” varies widely. Those describing a large number of patients with AS without operative therapy with necropsy findings are rare. Two hundred sixty patients >15 years of age with AS were studied at necropsy over a 50-year period by the same investigator. Of the 260 patients, the valve in 37 (14%) was congenitally unicuspid, in 123 (47%), congenitally bicuspid, and in 100 (38%), tricuspid. Aortic valve structure varied with age of death (in years; unicuspid 52 ± 17, bicuspid 63 ± 12, and tricuspid 70 ± 14 years); gender (men/women: unicuspid 95%/5%, bicuspid 78%/22%, and tricuspid 63%/37%), and frequency of calcium in the mitral valve annulus and epicardial coronary arteries. The patients with cardiac-related symptoms compared with those without were more likely to have a congenitally malformed valve (unicuspid 17% vs 12%; bicuspid 51% vs 29%; tricuspid 31% vs 60%; unadjusted P = 0.013), to die from cardiac disease (86% vs 54%; unadjusted P = 0.001), and to have larger hearts (mean cardiac weight 606 ± 138 g vs 523 ± 121 g; unadjusted P = 0.009) and a larger quantity of calcium in the aortic valve cusps. In conclusion, the length of survival in adults with AS is related to valve structure, gender, presence of cardiac-related symptoms, cardiac mass, and quantity of calcium in the aortic valve cusps.

Comparison of total 12-lead QRS voltage in a variety of cardiac conditions and its usefulness in predicting increased cardiac mass

Roberts WC, Filardo G, Ko JM, Siegel RJ, Dollar AL, Ross EM, Shirani J


Echocardiography provides a more accurate method to determine increased cardiac mass than does electrocardiography. Nevertheless, most offices of physicians do not possess echocardiographic machines, but many possess electrocardiographic machines. Many electrocardiographic criteria have been used to determine increased cardiac mass, but few of the criteria have been measured against cardiac weight determined at necropsy or after cardiac transplantation. Such was the purpose of the present study. Cardiac weight at necropsy or after transplantation was determined in 359 patients with 11 different cardiac conditions, and total 12-lead electrocardiographic QRS voltage (from the peak of the R wave to the nadir of either the Q or the S wave, whichever was deeper) was measured in each patient. Even in hearts with massively increased cardiac mass (>1,000 g), the total 12-lead QRS voltage was clearly increased (>175 mm) in only 94%, but this criterion was superior to that of previously described electrocardiographic criteria for “left ventricular hypertrophy.” Hearts with excessive adipose tissue infrequently had increased total 12-lead QRS voltage despite increased cardiac weight. Likewise, patients with fatal cardiac amyloidosis had hearts of increased weight but quite low total 12-lead QRS voltage. In conclusion, 12-lead QRS voltage is useful in predicting increased cardiac mass, but that predictability is dependent in part on the cause of the increased cardiac mass.

**ANESTHESIA AND ANALGESIA**

The accuracy, precision and reliability of measuring ventilatory rate and detecting ventilatory pause by rainbow acoustic monitoring and capnometry

Ramsay MA, Usman M, Lagow E, Mendoza M, Untalan E, DeVol E


Background: Current methods for monitoring ventilatory rate have limitations including poor accuracy and precision and low patient tolerance. In this study, we evaluated a new acoustic ventilatory rate monitoring technology for accuracy, precision, reliability, and the ability to detect pauses in ventilation, relative to capnometry and a reference method in postsurgical patients.

Methods: Adult patients presenting to the postanesthesia care unit were connected to a Pulse CO-Oximeter with acoustic monitoring technology (Rad-87, version 7804, Masimo, Irvine, CA) through an adhesive bioacoustic sensor (RAS-125, rev C) applied to the neck. Each subject also wore a nasal cannula connected to a bedside capnometer (Capnostream20, version 4.5, Oridon, Needham, MA). The acoustic monitor and capnometer were connected to a computer for continuous acoustic and expiratory carbon dioxide waveform recordings. Recordings were retrospectively analyzed by a trained technician in a setting that allowed for the simultaneous viewing of both waveforms while listening to the breathing sounds from the acoustic signal to determine inspiration and expiration reference markers within the ventilatory cycle without using the acoustic monitor- or capnometer-calculated ventilatory rate. This allowed the automatic calculation of a reference ventilatory rate for each device through a software program (TagEditor, Masimo). Accuracy (relative to the respective reference) and precision of each device were estimated and compared with each other. Sensitivity for detection of pauses in ventilation, defined as no inspiration or expiration activity in the reference ventilatory cycle for ≥30 seconds, was also determined. The devices were also evaluated for their reliability, i.e., the percentage of the time when each displayed a value and did not drop a measurement.

Results: Thirty-three adults (73% female) with age of 45 ± 14 years and weight 117 ± 42 kg were enrolled. A total of 3712 minutes of monitoring time (average 112 minutes per subject) were analyzed across the 2 devices; reference ventilatory rates ranged from 1.9 to 49.1 bpm. Acoustic monitoring showed significantly greater accuracy (P = 0.0056) and precision (P = 0.0024) for respiratory rate as compared with capnometry. On average, both devices displayed data over 97%
likely related to fat necrosis than recurrent tumor. Acoustic monitoring was marginally more sensitive ($P = 0.0461$) to pauses in ventilation (81% vs 62%) in 21 apneic events.

**Conclusions:** In this study of a population of postsurgical patients, the acoustic monitor and capnometer both reliably monitored ventilatory rate. The acoustic monitor was statistically more accurate and more precise than the capnometer, but differences in performance were modest. It is not known whether the observed differences are clinically significant. The acoustic monitor was more sensitive to detecting pauses in ventilation. Acoustic monitoring may provide an effective and convenient means of monitoring ventilatory rate in postsurgical patients.

**ASAIO JOURNAL**

**Case series using the ROTAFLOW system as a temporary right ventricular assist device after HeartMate II implantation**

Khani-Hanjani A, Loor G, Chamogeorgakis T, Shafii A, Mountis M, Hanna M, Soltész E, Gonzalez-Stawinski GV


The purpose of this study was to investigate the outcomes of using the ROTAFLOW as a temporary right ventricular assist device (RVAD) support in patients who develop right ventricular dysfunction (RVD) at the time of left ventricular assist device (LVAD) implantation with the HeartMate (HM) II. We conducted a retrospective chart review of patients in whom the ROTAFLOW system was used for RV support during HM II implantation from October 2009 to September 2011. Twelve patients received a ROTAFLOW as an RVAD at the time of HM II implantation; 83% had preoperative echocardiography evidence of either moderate or severe RVD. The most common complications in the postoperative period were the need for tracheostomy because of respiratory failure (45%) and mediastinal bleeding requiring exploration (36%). Ninety-one percent of patients survived to discharge, and all were alive at 1 year follow-up. Our results show that temporary RVAD support with the ROTAFLOW system in the setting of RVD at the time of HM II implantation is feasible and effective.

**CLINICAL NUCLEAR MEDICINE**

**Diffuse FDG uptake due to fat necrosis following transverse rectus abdominus myocutaneous (TRAM) flap reconstruction**

Dobbs NB, Latifi HR


We report a case of a 57-year-old female patient with right breast invasive ductal carcinoma. Bilateral mastectomy and TRAM flap reconstructions were performed. Postoperatively, a palpable focus was identified within the left breast. PET/CT showed hypermetabolism throughout the reconstructed left breast, correlating with mixed fat attenuation and inflammatory soft tissue. MRI showed extensive fat necrosis/oil cyst formation in the left breast. As a TRAM flap reconstruction with fat-rich tissue can be damaged intraoperatively due to surgical manipulation, abnormal FDG uptake in this setting is more likely related to fat necrosis than recurrent tumor.

**CONTEMPORARY CLINICAL TRIALS**

**Chronic obstructive pulmonary disease self-management activation research trial (COPD-SMART): design and methods**

Ashmore J, Russo R, Peoples J, Sloan J, Jackson BE, Bae S, Singh KP, Blair SN, Coultas D


**Background:** Treatment of COPD requires multiple pharmacological and non-pharmacological intervention strategies. One target is physical inactivity because it leads to disability and contributes to poor physical and mental health. Unfortunately, less than 1% of eligible patients have access to gold-standard pulmonary rehabilitation.

**Methods:** A single-site parallel group randomized trial was designed to determine if a self-management lifestyle physical activity intervention would improve physical functioning and dyspnea. During the first 6 weeks after enrollment, patients receive COPD self-management education delivered by a health coach using a workbook and weekly telephone calls. Patients are then randomized to usual care or the physical activity intervention. The 20-week physical activity intervention is delivered by the health coach using a workbook supported by alternating one-on-one telephone counseling and computer assisted telephone calls. Theoretical foundations include social cognitive theory and the transtheoretical model.

**Results:** Primary outcomes include change in Chronic Respiratory Questionnaire (CRQ) dyspnea domain and 6-minute walk distance measured at 6, 12, and 18 months after randomization. Secondary outcomes include other CRQ domains (fatigue, emotion, and mastery), SF-12, and health care utilization. Other measures include process outcomes and clinical characteristics.

**Conclusions:** This theory-driven self-management lifestyle physical activity intervention is designed to reach patients unable to complete center-based pulmonary rehabilitation. Results will advance knowledge and methods for dissemination of a potentially cost-effective program for patients with COPD.

**FOOT AND ANKLE INTERNATIONAL**

**Prospective study of the treatment of adult primary hallux valgus with scarf osteotomy and soft tissue realignment**

Choi JH, Zide JR, Coleman SC, Brodsky JW


**Background:** The scarf osteotomy has been a widely practiced bunion operation, but relatively limited prospective data on its outcomes have been reported. The purpose of this investigation was to prospectively evaluate the clinical and radiographic results of treatment of adult primary hallux valgus using the scarf osteotomy of the first metatarsal with soft tissue realignment.

**Methods:** Hallux valgus corrections were performed on 51 patients (53 feet), who were followed for at least 1 year with an average follow-up of 24 months. Mean age at the time of surgery was 59 years, and subjects included 3 male and 48 female patients. Prospective clinical data collected included the American Orthopaedic Foot & Ankle Society (AOFAS) hallux-interphalangeal scale score,
the SF-36 scores, and the visual analogue scale (VAS) for pain. Data were collected preoperatively and postoperatively. Prospective radiologic data were also collected including hallux valgus angle (HVA), first-second intermetatarsal angle (IMA), and medial sesamoid position (MSP). Clinical data were collected on complications and reoperations.

**Results:** Mean AOFAS hallux-interphalangeal score increased from 52 preoperatively to 88 postoperatively. Mean preoperative and last follow-up SF-36 physical component summary increased from 46 preoperatively to 52 postoperatively, whereas mean VAS pain scores decreased from 5.8 preoperatively to 1.1 postoperatively. All the changes in clinical outcomes were statistically significant, except the Mental Component Summary of the SF-36. Mean preoperative HVA decreased from 29 degrees preoperatively to 10.7 degrees in the initial postoperative period and was maintained at last follow-up at 10.6 degrees. The mean preoperative IMA decreased from 13.6 degrees preoperatively to 5.6 degrees in the initial postoperative period and regressed mildly at last follow-up to 7.8 degrees. The mean preoperative MSP grade of 2.3 decreased to 0.5 in the initial postoperative period and regressed mildly to 0.9 at last follow-up. All radiographic changes were statistically significant. The overall complication rate was 15% (8/53), attributable to 4 feet with symptomatic hardware, 2 feet with hallux varus, and 2 feet with progression of first MTP arthritis. Reoperations were performed in 4 feet (8%) for removal of symptomatic hardware.

**Conclusion:** Scarf osteotomy was a reliable technique for correction of moderate to severe hallux valgus and had low rates of complication or recurrence.

**Level of evidence:** Level IV, case series.

**Hindfoot motion following STAR total ankle arthroplasty: a multisegment foot model gait study**

Brody JW, Coleman SC, Smith S, Polo FE, Tenenbaum S


**Background:** One of the rationales for total ankle arthroplasty (TAA) is that it may retard the changes of hypermobility and accelerated arthritis in the hindfoot after ankle arthrodesis. Until recently, it has not been possible to quantify or even objectively demonstrate biomechanical findings to substantiate the theory that postsurgical biomechanical changes in the ankle produce changes in the kinematics of the hindfoot. Standard gait analysis has treated the foot as a single biomechanical unit. This study was undertaken to describe the hindfoot motion following Scandinavian Total Ankle Replacement (STAR) TAA by using multisegment foot model gait analysis.

**Methods:** Forty-six patients with a mean age of 66 years underwent a 3D gait analysis following TAR. Mean interval between surgery and gait analysis was 4.9 years (range 2 to 9). The contralateral limb was used as control for each patient. Temporospatial variables and kinematic parameters were studied.

**Results:** Temporospatial results showed statistically significant differences. Stance time on the affected side was 61.1% ± 2.2% of the gait cycle compared to 63.2% ± 2.1% for the unaffected side. Step length was 55.6 cm ± 10 on the affected side compared to 53.9 cm ± 10 for the unaffected side. Kinematics results were statistically significant: Ankle range of motion (ROM) on the arthroplasty side was 16.8 ± 4.5 degrees compared to 23.6 ± 5.0 on the unaffected side. Sagittal plane ROM was 12.7 ± 4.2 degrees on the arthroplasty side and 17.3 ± 3.5 degrees on the unaffected side. Coronal plane ROM was 4.7 ± 2.4 degrees on the arthroplasty side and 7.5 ± 2.4 degrees on the unaffected side. Transverse plane ROM on the arthroplasty side was 4.1 ± 1.5 degrees and 4.9 ± 1.6 on the unaffected side.

**Conclusion:** This study showed that, in addition to previously documented diminution in sagittal plane motion and gait velocity, some of the residual abnormalities of gait following TAR were comprised of differences in hindfoot function. These results relate to the growing recognition of the importance of understanding hindfoot mechanics apart from those of the tibiotalar joint.

**Level of evidence:** Level III, comparative case series.

---

**GUT**

Hypomethylation of long interspersed nuclear element-1 (LINE-1) leads to activation of proto-oncogenes in human colorectal cancer metastasis

Hur K, Cejas P, Feliu J, Moreno-Rubio J, Burgos E, Boland CR, Goel A

*Gut* 2013 May 23 [Epub ahead of print]. Reprinted with permission from BMJ Publishing Group Ltd.

**Objective:** Hypomethylation of LINE-1 elements has emerged as a distinguishing feature in human cancers. Limited evidence indicates that some LINE-1 elements encode an additional internal antisense promoter, and increased hypomethylation of this region may lead to inadvertent activation of evolutionarily methylation-silenced downstream genes. However, the significance of this fundamental epigenetic mechanism in colorectal cancer (CRC) has not been investigated previously.

**Design:** We analysed tissue specimens from 77 CRC patients with matched sets of normal colonic mucosa, primary CRC tissues (PC), and liver metastasis tissues (LM). LINE-1 methylation levels were determined by quantitative bisulphite pyrosequencing. MET, RAB3IP and CHRM3 protein expression was determined by western blotting and IHC. MET proto-oncogene transcription and 5-hydroxymethylcytosine (5-hmc) were evaluated by quantitative real-time PCR.

**Results:** Global LINE-1 methylation levels in LM were significantly lower compared with the matched PC (PC = 66.2% vs LM = 63.8%; P < 0.001). More importantly, we observed that specific LINE-1 sequences residing within the intronic regions of multiple proto-oncogenes, MET (P < 0.001), RAB3IP (P = 0.05), and CHRM3 (P = 0.01), were significantly hypomethylated in LM tissues compared with corresponding matched PC. Furthermore, reduced methylation of specific LINE-1 elements within the MET gene inversely correlated with induction of MET expression in CRC metastases (R = -0.44; P < 0.0001). Finally, increased 5-hmc content was associated with LINE-1 hypomethylation.

**Conclusions:** Our results provide novel evidence that hypomethylation of specific LINE-1 elements permits inadvertent activation of methylation-silenced MET, RAB3IP, and CHRM3 proto-oncogenes in CRC metastasis. Moreover, since 5-hmc content inversely correlated with LINE-1 hypomethylation in neoplastic tissues, our results provide important mechanistic insights into the fundamental processes underlying global DNA hypomethylation in human CRC.


**IMMUNITY**

Systems scale interactive exploration reveals quantitative and qualitative differences in response to influenza and pneumococcal vaccines


Systems immunology approaches were employed to investigate innate and adaptive immune responses to influenza and pneumococcal vaccines. These two non-live vaccines show different magnitudes of transcriptional responses at different time points after vaccination. Software solutions were developed to explore correlates of vaccine efficacy measured as antibody titers at day 28. These enabled a further dissection of transcriptional responses. Thus, the innate response, measured within hours in the peripheral blood, was dominated by an interferon transcriptional signature after influenza vaccination and by an inflammation signature after pneumococcal vaccination. Day 7 plasmablast responses induced by both vaccines were more pronounced after pneumococcal vaccination. Together, these results suggest that comparing global immune responses elicited by different vaccines will be critical to our understanding of the immune mechanisms underpinning successful vaccination.

**JOURNAL OF SPINAL DISORDERS AND TECHNIQUES**

Retrospective study of anterior interbody fusion rates and patient outcomes of using mineralized collagen and bone marrow aspirate in multilevel adult spinal deformity surgery


**Design:** Retrospective, single-center analysis of multilevel anterior fusion rates and health-related quality-of-life (HRQOL) outcomes of mineralized collagen and bone marrow aspirate (BMA) in anterior interbody fusion cages for spine fusion surgery.

**Objective:** To determine the ability and effectiveness of mineralized collagen and BMA to achieve multilevel anterior spinal fusion in adult spinal deformity patients when placed in carbon fiber reinforced polymer cages.

**Summary of background data:** High rates of post-operative pain and non-union can result from spine fusion procedures. Factors that affect the success of fusion include patient co-morbidities, position of implant, and mechanical and biologic deficiencies, as well as the choice of bone graft replacement.

**Methods:** Analysis of radiographic images and HRQOL outcomes was performed for a consecutive series of 22 prospectively enrolled adult spinal deformity patients with 104 total anterior fusion levels. Fusions were graded by 3 blinded surgeons not involved in the operative procedure; each fusion was graded on a 1–4 scale based on fusion mass appearance. Levels with an average fusion grade of 1–2.4 were classified as fused; levels with an average grade >2.5 were classified as not fused.

**Results:** The mean patient age was 51.5 years (range 38–61) with 21 females; 95% of anterior operative levels were graded as fused based on flexion/extension and full length biplane radiographs at one year. CT grading showed a reduced fusion rate at 87% overall. There was a statistically significant improvement in the Oswestry Disability Index and Scoliosis Research Society 22-item questionnaire scores at one year and two years following index surgery.

**Conclusions:** Fusion rates in multilevel anterior spinal fusion using mineralized collagen and BMA are relatively low compared to fusion rates of 95% or more reported in the existing literature on long fusions with BMP.

**LIVER TRANSPLANTATION**

Preformed class II donor-specific antibodies are associated with an increased risk of early rejection after liver transplantation

O’Leary JG, Kaneku H, Jennings LW, Bañuelos N, Susskind BM, Terasaki PI, Klintmalm GB


Preformed donor-specific human leukocyte antigen antibodies (DSAs) are considered a contraindication to the transplantation of most solid organs other than the liver. Conflicting data currently exist on the importance of preformed DSAs in rejection and patient survival after liver transplantation (LT). To evaluate preformed DSAs in LT, we retrospectively analyzed prospectively collected samples from all adult recipients of primary LT without another organ from January 1, 2000 to May 31, 2009 with a pre-LT sample available (95.8% of the patients). Fourteen percent of the patients had preformed class I and/or II DSAs with a mean fluorescence intensity (MFI) >5000. Preformed class I DSAs with an MFI>5000 remained persistent in only 5% of patients and were not associated with rejection. Preformed class II DSAs with an MFI of 5000 to 10,000 remained persistent in 23% of patients, and this rate increased to 33% for patients whose MFI was >10,000 (P <0.001). Preformed class II DSAs in a multivariate Cox proportional hazards modeling were associated with an increased risk of early rejection [hazard ratio (HR) = 1.58]. In addition, multivariate modeling showed that in comparison with no DSAs (MFI<1000), preformed class I and/or II DSAs with an MFI>5000 were independently correlated with the risk of death (HR = 1.51).

**MOLECULAR GENETICS AND METABOLISM**

Quantitation of gamma-hydroxybutyric acid in dried blood spots: Feasibility assessment for newborn screening of succinic semialdehyde dehydrogenase (SSADH) deficiency

Forini S, Pearl PL, Gibson KM, Yu Y, Sweetman L


**Objective:** SSADH deficiency, the most prevalent autosomal recessive disorder of GABA degradation, is characterized by elevated gamma-hydroxybutyric acid (GHB). Neurological outcomes may be improved with early intervention and anticipatory guidance. Morbidity has been...
compounded by complications, e.g. hypotonia, in undiagnosed infants with otherwise routine childhood illnesses. We report pilot methodology on the feasibility of newborn screening for SSADH deficiency.

**Method:** Dried blood spot (DBS) cards from patients affected with SSADH deficiency were compared with 2831 archival DBS cards for gamma-hydroxybutyric acid content. Following extraction with methanol, GHB in DBS was separated and analyzed using ultra high-performance liquid chromatography tandem mass spectrometry.

**Results:** Methodology was validated to meet satisfactory accuracy and reproducibility criteria, including intra-day and inter-day validation. Archival refrigerated dried blood spot samples of babies, infants, and children (N = 2831) were screened for GHB, yielding a mean ± S.D. of 8 ± 5 nM (99.9%-tile 63 nM) (Min 0.0 Max 78 nM). The measured mean and median concentrations in blood spots derived from seven SSADH deficient patients were 1182 nM and 699 nM respectively (Min 124, Max 4851 nM).

**Conclusions:** GHB concentration in all 2831 dried blood spot cards was well below the lowest concentration of affected children. These data provide proof-of-principle for screening methodology to detect SSADH deficiency with applicability to newborn screening and earlier diagnosis.

**WORLD JOURNAL OF SURGERY**

Resection of at-risk mesenteric lymph nodes is associated with improved survival in patients with small bowel neuroendocrine tumors


**Background:** Neuroendocrine tumors of the small intestine commonly metastasize to regional lymph nodes (LN). Single-institution reports suggest that removal of LN improves outcome, but comprehensive data are lacking. We hypothesized that the extent of lymphadenectomy reported in a large administrative database would be associated with overall survival for jejunal and ileal neuroendocrine tumors.

**Methods:** A search of the Surveillance Epidemiology and End Results database was performed for patients with jejunal and ileal neuroendocrine tumors from 1977 to 2004. Descriptive patient characteristics were collected to include age at diagnosis, sex, race, grade, primary tumor size, LN status, number of LNs resected, presence of distant metastasis, and the type of operation. Statistical analyses were limited to patients with only one primary tumor to exclude patients with other malignancies. Univariate and multivariate analyses were performed to analyze the number of LNs resected and the LN ratio (number of positive LNs/total number of LNs removed) to determine the effect on cancer-specific survival.

**Results:** Altogether, 1,364 patients were included in this analysis. Removal of any LNs was associated with improved cancer-specific survival when compared to patients with no LN removal reported (P = 0.0027) on univariate analysis. Among those who had any LNs removed, a median of eight LNs were identified in resection specimens with a median LN ratio of 0.29 (range 0–1). On multivariate analysis (adjusting for age and tumor size), patients with >7 LNs removed experienced better cancer-specific survival than those with ≤7 LNs removed (median survival not reached vs. 140 months): hazard ratio and 95% confidence interval were 0.573 (0.402, 0.817) (P = 0.002).

**Conclusions:** This review of a large number of surgical patients demonstrates that regional mesenteric lymphadenectomy in conjunction with resection of the primary tumor is associated with improved survival of patients with small bowel neuroendocrine tumors.
Instructions for authors

Baylor University Medical Center Proceedings welcomes research articles, review articles, case studies, and editorials from Baylor and non-Baylor authors. Manuscripts containing Baylor data are particularly desired. Send all manuscripts and editorial correspondence to William C. Roberts, MD, Editor in Chief, Baylor Scientific Publications Office, 3500 Gaston Avenue, Dallas, Texas 75246; phone: 214-820-9996; fax: 214-820-4064; e-mail: cynthiao@BaylorHealth.edu.

MANUSCRIPT SUBMISSION

Submit the word processing document by e-mail to cynthiao@BaylorHealth.edu. Large files may be sent using YouSendIt or SendNow.

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

Schedule: Deadlines for submission are as follows: January issue, September 1; April issue, December 1; July issue, March 1; and October issue, June 1. The editorial office cannot guarantee that any manuscript submitted by these deadlines will be published in the specified issue; variables include the peer review and revision process and the number of articles already accepted.

ARTICLE TYPES

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

Case studies: Include an abstract, a single-paragraph introduction (optional with short reports), a case description of 0.5 to 2 double-spaced pages, and a discussion of 1 to 5 double-spaced pages. Up to 25 references are acceptable (although many case reports have 5 to 10). The maximum number of figures and tables (combined) is 6.

Historical studies: Abstracts are recommended. There is no word limit, but most historical studies are 1500 to 3500 words.

Editorials: There is no word limit, but most editorials are 800 to 1600 words.

Book reviews: See past issues for format. There is no word limit, but most book reviews are 800 to 1600 words.

Avocations: Submit an image file for your painting or photograph or a discussion of your hobby for a maximum of 300 words.

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

MANUSCRIPT PREPARATION

Format: Type manuscripts double spaced, leaving 1-inch margins. Number all pages, including the title page.

Title page: Include on the first page the article’s title; the authors’ names, highest degree(s), and affiliations; and the name, address, e-mail address, and phone number of the corresponding author. Acknowledge any grant support.

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

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

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


Authors using Endnote can access Proceedings’ reference style by downloading an EndNote style file, available at http://www.baylor-health.edu/Research/Proceedings/SubmitaManuscript/Pages/ManuscriptPreparation.aspx. Personal communications and unpublished data should not be used as references; they should be identified in parentheses in the text.

Tables and figures: Number tables and figures in the order in which they are discussed in the text. Include call-outs in the text and place the tables at the end of the document as Word files using the Word table function. Figures can be embedded in the text at the end of the document or provided as separate files, with legends in the Word file. Provide enough details in titles, footnotes, and legends so that the tables and figures can be understood apart from the text. Submit photographs as 350-ppi tiff or jpeg files. Submit graphs and diagrams as electronic files (EPS format preferred).

Use of color: Color is used in articles only when clinically required (as with certain pathology and radiology images). Avoid using color when creating charts and graphs. If photographs (such as those in interviews) are originally in color, they can be converted to black and white during journal production. Articles that use color are generally grouped together in the issue to decrease overall printing expenses.

Style issues: Use generic names for drugs; capitalize any trade names when they are used. Limit the number of abbreviations in a manuscript to five, and do not abbreviate single words, such as intravenous. Spell out all abbreviations on first usage. Proceedings
follows the style guide of the American Medical Association. As further guidance, prospective authors are encouraged to consult the “Authors’ submission toolkit” (1) and an article on medical publishing by the editor in chief (2).

MANUSCRIPT PROCESSING

Peer review: All manuscripts are subject to peer review by editorial board members or other selected reviewers; however, the final decision as to which articles are published will be made by the editor in chief. At the time of manuscript submission, authors are encouraged to suggest reviewers, within or outside the Baylor Health Care System, and to list any reviewers they feel should not be used because of potential bias. If a manuscript was previously reviewed by another journal, authors should submit those reviews and clearly indicate any revisions that have been made. Such manuscripts will receive expedited processing, since they usually will not be sent out for re-review.

Editing: All manuscripts will be edited for clarity and conformity to Proceedings’ style. The corresponding author will have the opportunity to review editing either before or at the page proof stage.

Reprints: Authors can order reprints using the form provided through an e-mail link from the printer. Reprints are delivered approximately 4 weeks after the issue comes out. All authors receive a copy of the printed journal, and PDF files of articles are freely available to the authors and the general public.

JOURNAL POLICIES

Duplicate publication: When submitting the manuscript, provide a copy of any published or submitted article that is similar to what is being submitted to Proceedings, so that the editor can judge whether the manuscript in question would be a duplicate publication. Once manuscripts are accepted, authors transfer copyright to Baylor University Medical Center at Dallas.

Authorship: All authors listed in the manuscript must have participated in the design or analysis of the project. In addition, all authors must review the final text and be prepared to take public responsibility for its content.

Ethical treatment of research subjects: For reports of experimental investigations of human or animal subjects, indicate institutional review board approval or exemption within the manuscript. Authors should also explain in the Methods section the procedures followed to obtain informed consent.

Conflict of interest: Grant support for a particular study must be indicated on the title page. In addition, authors must communicate to the editor in the cover letter any affiliations that could be perceived as potential conflicts of interest. Examples include honoraria, educational grants, participation in speakers’ bureaus, expert testimony, patent licensing arrangements, consultancies, and stock ownership.

Use of protected health information: Authors should not refer to patients by name or initials or provide other specific identifying information, such as Social Security number or medical record number. Authors are further encouraged to avoid including extraneous social details about patients. Patient authorization forms are required for all identifying photographs. For a copy of Proceedings’ full privacy policy, contact the managing editor.

Permissions: Permission is required for reproduction of any material, including figures and tables, that has been published elsewhere. When submitting manuscripts, provide written documentation that permission has been obtained or notify the editorial staff of the need to request permission (providing all necessary source information). For photographs in which the subject can be recognized, submit release authorizations at the time of manuscript submission.

For additional information, please contact Cynthia Orticio, managing editor, at 214-820-9996 or cynthiao@BaylorHealth.edu.

Fibromuscular dysplasia of the renal artery as a cause of secondary hypertension
A. Y. Hundae, C. A. Hebert, and J. M. Schussler

Slow group beating
D. L. Glancy and V. N. Lathia

Continuous murmur and cardiac failure in a 53-year-old woman
D. L. Glancy and E. B. Hanna

Amiodipine overdose
T. Patel, D. Tenzer, and A. N. Mehta

Historical Studies
417 Consults for conflict: the history of ethics consultation
Elliot B. Tapper

Editorials
423 What’s going on in dental education?
Eric S. Solomon

An unforgettable, perpetual medical student, 1961
S. Robert Lathan

Book Reviews
427 Review of For the Love of Wild Things (Dimijian)
Daniel E. Polter

428 Review of Sifting Shades (Khan)
Harbans Lal

From the Editor
432 Facts and ideas from anywhere
William C. Roberts

Miscellany
386 Aversions: Photograph by Dr. Roseenthal
412 Baylor news
416 Clinical research studies enrolling patients
429 Reader comments: Cardiac rehabilitation in firefighters
442 Selected published abstracts of Baylor researchers
447 Instructions for authors