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California. More of Ms Balian’s art can be found on the Web site: www.marshabalian.com.

In a retrospective review, 1015 continuous patients with suspected deep vein thrombosis (DVT) were clinically evaluated in a laboratory with a D-dimer assay. 753 with a bistheria system and 512 with a Trinity Biotech system. With the Trinity Biotech assay specificity increased from 41.3% to 66.9%, positive predictive value increased 2.5 times from 8.8% to 20.0%, and the probability of DVT increased from 29% to 58%. A significant number of unnecessary compression ultrasonograms were saved.

From Our Lips To Whose Ears?: Consumer Reaction to Our Current Health Care Dialet, Murray Ross, PhD, Toyotchi Iga, Sophia Gomez

Bimanual palpation of the testicles in young men is a standard physical examination [1] but little is known about patient reaction to the language used in this examination. The Permanente Medical Group (PMG) is a large, multi-specialty group, practicing prepaid health care, and its members include: “communication,” “treatment,” “guidelines,” “invasive testing and imaging” and “best practices.”

The hematologist, however, this qualitative study, conducted with consumers from Boston, New York City, St Paul, Billings, and San Diego, revealed a tremendous gap between what healthcare consumers hear, and what healthcare professionals say and do. Consequently, many patients with microscopic or gross hematuria unreferral (HLA, ABO, CHE)

Hematoma: How to Evaluate in the Absence of Strong Evidence? Ronald Liss, MD; Joel Whitaker, MPH; Violeta Rabrenivich, MHA, CHE

Hematuria is one of the most common conditions confronting clinical urologists, and generalists, however the existing lack of scientific evidence has created variations in clinical practice. Consequently, many patients with microscopic or gross hematuria undergo low-yield workups that include invasive testing and imaging with radiation. As a response, a national group of KP urology chiefs developed national practice recommendations.

Laparoscopic Surgery for Rectal Cancer. Adrian Indar, MD; MBBS, FICS, DABR; Jonathan Efron, MD, FACS, FASCR

Because of the confined space within the pelvis, laparoscopic surgery for rectal cancer is much more challenging than that for colon cancer, particularly maintenance of resection margins. Nonrandomized studies have shown that this produces short-term outcomes equivalent to open surgery, performed safely from an oncologic perspective. This review summarizes the technical considerations, early outcomes, late outcomes, and complications.
CASE STUDIES

53 A Case of Large Pericardial and Pleural Effusions Associated With Pulmonary Emboli in a User of Crack Cocaine.
Hien Nguyen, MD; Connie Le, MD; Hanh Nguyen, MD

This is an unusual case of a user, age 56 years, of crack cocaine who presented with progressive dyspnea of subacute duration. One prior case report describes the development of a pleural effusion via an eosinophilic process. In contrast, in this patient the most probable mechanism is that crack cocaine induced a prothrombotic state that promoted formation of pulmonary emboli.

57 Recognition of Kawasaki Disease.
Janelle R Cox, MD; Robert E Sallis, MD

One of the most common vascularities of childhood is the leading cause of acquired heart disease in children in the US. Though it should be included in the differential diagnosis for any child with prolonged fever that is unresponsive to antibiotics, the diagnosis is often difficult in that the symptoms tend to present at different times, and require multiple examinations on different days.

CLINICAL MEDICINE

62 The B-SMART Appropriate Medication-Use Process: A Guide for Clinicians to Help Patients—Part 1: Barriers, Solutions, and Motivation. Elizabeth Oyekan, PharmD, FCSPH; Ananda Nimalasuriya, MD; John Martin, MD; Ron Scott, MD; R James Duld, MD; Kelley Green, RN, PhD

This multifaceted approach used before, during, and after any patient-clinician interaction creates a consistent method to help patients more effectively use their medications. Elements include: involving patients in the decision-making, simplifying dosage regimens, education about the medication, self-management training, ongoing reinforcement and motivation, and positive relationships. Concrete solutions are provided to nine common practice challenges, including: forgetfulness, literacy, denial, financial, depression, and lack of knowledge.

70 Image Diagnosis: Foot Fractures. Gus M Garvel, MD, FACEP, FAEM

Although it may be difficult to see a Lisfranc foot fracture, significant force is needed to disrupt and dislocate this strong joint which stabilizes the mid-foot. Calcaneus fractures, also the result of significant force can be associated with vertebral body fractures of the spine.

73 Evaluation of Hypertension with Hypokalemia. Antoine C Abcar, MD; Dean A Kujubu, MD

Hypertension that remains in poor control despite the use of many medications is a difficult problem that every primary care physician has faced. This article focuses on those less common causes of hypertension with hypokalemia—essential hypertension with diuretic use, primary aldosteronism, Cushing’s syndrome, pheochromocytoma, renal vascular disease, and malignant hypertension.

Commentary

78 SCPMG University: Helping New Physicians Adapt and Succeed. Jeffrey Weisz, MD; Nancy H Spiegel, MS

An individual’s first few months with an organization are crucial. During that period, professionals develop a sense of what is important, what the organization expects from them, and what they can expect in return. Mean scores, from first-year, pre- to postprogram surveys, improved significantly on 11 of 14 items demonstrating the success of the University program in helping physicians adapt to their new positions, thus laying the foundation for a successful career within the medical group.

87 At a Decade: Centers of Excellence in Culturally Competent Care. Melanie Tevalon, MD, MPH

Rapidly increasing national racial and ethnic diversity calls for interventions that are culturally specific to improve patients’ health outcomes and to eliminate health disparities. Kaiser Permanente developed nine innovative Centers of Excellence in Culturally Competent Care that are population-based, data-driven research projects that unravel and explain the dynamic processes by which culture, race, and ethnicity interact in health care delivery settings.

Narrative Medicine

80 Narrative-Based Medicine: Potential, Pitfalls, and Practice. Vera Kalitzkus, PhD; Peter F Matthiessen, MD, PhD

With the evolution of “modern” medicine, narratives were increasingly neglected in favor of “facts and findings,” regarded as more scientific and objective. Now—through understanding the narrative structure of medical knowledge, and narrative-oriented, physician-patient relations—narratives from social science research and medical practice and patient encounters are a source of knowledge for evidence, beyond the gold standard of randomized controlled trials of evidence-based medicine. This is a systematic overview of narrative-based medicine—background, narrative genres, and application in theory, research, and medical practice.

94 The Desert Doctor. Tom Debley

This is the first chapter from the new book published by The Permanente Press—The Story of Dr Sidney R Garfield: The Visionary Who Turned Sick Care Into Health Care—documenting the creation of Kaiser Permanente by cofounders Sidney Garfield and Henry J Kaiser. This biography, focuses, for the first time, on Sidney Garfield’s story and vision.
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The Kaiser Permanente National Continuing Medical Education Program (KPNCMEP) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. The KPNCMEP designates this educational activity for 4 AMA PRA Category 1 credits. Each physician should claim only those hours of credit that s/he actually spent in the educational activity. All authors in this issue report no conflict of interest.

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Improving D-dimer Positive Predictive Value for Outpatients with Suspected Deep Vein Thrombosis

Craig M Nelson, PhD, CLS
Geary S Wright, BA, MLT
Tom R Silbaugh, CPT
Louis J Cota, CLS

Abstract

Context: Sensitive D-dimer assays have been developed to exclude the diagnosis of deep vein thrombosis (DVT) and have exhibited great success when used in conjunction with a diagnostic algorithm, including pretest probability scoring and a compression ultrasound (CUS). Improving specificity of D-dimer assays would significantly improve the utility of CUSs.

Objective: Our objective was to evaluate the ability of a new D-dimer assay to improve specificity, positive predictive ability, and Bayesian probability when compared with an assay previously used in our laboratory.

Methods: We retrospectively reviewed 1015 continuous patients with suspected DVT. All patients were clinically evaluated in our laboratory with a D-dimer assay: 503 were clinically evaluated with a bioMérieux D-dimer test system and 512 were evaluated with a Trinity Biotech D-dimer test system. Outcomes were assessed statistically using sensitivity, negative predictive value, Bayesian negative probability, specificity, positive predictive value, and Bayesian positive probability.

Results: The data for our study showed that with the Trinity Biotech D-dimer assay, specificity increased from 41.3% to 66.9%, positive predictive value increased 2.3 times from 8.8% to 20.0%, and the probability of DVT after positive results on a D-dimer test increased from 25% to 38% when compared with the bioMérieux D-dimer test system. In addition to the improved parameters for clinical performance, a significant number of unneeded CUSs were saved. The number of false positive D-dimer assays significantly decreased and positive predictive ability improved when the Trinity Biotech test system was used in our laboratory.

Introduction

Deep vein thrombosis (DVT) causes thousands of patients in the US to be hospitalized each year, and many more instances of DVT are diagnosed while patients are hospitalized for surgical procedures or medical illness.

Prompt diagnosis of DVT and treatment prevent the short-term onset of pulmonary embolism and death, the long-term complications of recurring venous thromboembolism, and the complications of post-thrombotic syndrome.

The objective diagnosis of DVT relies on highly sensitive and specific compression ultrasonography (CUS) or ascending venography. The cost of these modalities and the incidence of negative test findings have led to alternative approaches to diagnosis and decision making in suspected cases of DVT. These rely on the use of diagnostic information from clinical history, examination, and assays to detect D-dimers.

Sensitive D-dimer assays have been developed to exclude the diagnosis of DVT and have exhibited great success when used in conjunction with a diagnostic algorithm, including pretest probability scoring and CUS. A value of >500 ng/mL has been established by our laboratory as a positive D-dimer result. In conjunction with a low to moderate pretest probability, a CUS is ordered. For those patients with a high pretest probability, a CUS is ordered without the D-dimer assay being done. With the combination of pretest probability and D-dimer assay, both a sensitivity and negative predictive value >96% has been established in the literature and has been duplicated by our laboratory.
The object of this study, approved by the Kaiser Permanente (KP) Southern California Institutional Review Board, was to test whether the positive predictive value, specificity, and Bayesian positive probability of the D-dimer assay was improved by the use of a Trinity Biotech latex-enhanced immunoassay in place of the previous bioMérieux assay used in our laboratory. We also hoped to discover whether improvement in sensitivity, negative predictive value, and Bayesian negative probability occurred when using the new latex-enhanced immunoassay. In addition, we believe that our data will provide a clear understanding of whether the Trinity Biotech latex-enhanced immunoassay enabled a more efficient use of CUS than the bioMérieux did.

Methods
We retrospectively reviewed 1015 continuous outpatients suspected of DVT who were seen in the KP Medical Center in Fontana, CA, between January 2007 and April 2008. We also included in our data a three-month follow-up review of all patients to determine whether any patient presented with a delayed positive DVT. The three-month follow-up assessment involved chart or electronic medical record review for all 1015 patients. We excluded inpatients and residents of skilled nursing facilities for whom the false positive rate of the D-dimer assay was markedly high. The excluded patient population included elderly patients, pregnant patients, and those with cancer or autoimmune diseases. The patients reviewed for this study were referred from primary care clinics, the Emergency Department, surgery clinics, and the Ob/Gyn Department for DVT. For all 1015 patients, we used a diagnostic algorithm including pretest probability scoring to assess clinical likelihood of DVT; those with low to moderate probability scores were deemed candidates for D-dimer analysis. Of the 1015 continuous outpatients suspected of having DVT, 503 patients were tested with the bioMérieux quantitative homogeneous-phase latex D-dimer immunoassay (bioMérieux, Marcy l’Etoile, France) and 512 were tested with the Trinity Biotech immunoturbidimetric latex Auto-dimer immunoassay (Trinity Biotech, Wicklow, Ireland) and an MDA II analyzer (Trinity Biotech). The cost per D-dimer test was the same for both assays.

The bioMérieux assay uses a Mab8-8G monoclonal antibody and a wavelength of 580 nm. The Trinity Biotech latex-enhanced immunoassay combines an MA-8D3 monoclonal antibody and a size-adjusted latex bead so that the 660-nm wavelength used for the assay remains two times the size of the bead. This is reported by the manufacturer to ensure that the particle will have its maximum absorption. The combination of size-adjusted latex bead, MA-8D3 monoclonal antibody, and higher wavelength were reported to increase analytic sensitivity and assay range (Kevin J McGlinchey, MT (ASCP), CLS (CG), Marketing Manager, Instrumentation, Trinity Biotech, personal communication, April 24, 2008).

Our study postulated that with the Trinity Auto-dimer assay, there should be an increased level of specificity and positive predictive value and an increased cost efficiency of the assay by reducing the number of negative images.

To determine the clinical performance of both assays, we used six statistical assessments: sensitivity, negative predictive value, specificity, positive predictive value, and Bayes’s theorem for both positive and negative post-test DVT probability.

Results
Table 1 shows the parameters used for evaluating the clinical performance of the D-dimer assays used to exclude the diagnosis of DVT. The 503 patients for whom the bioMérieux test system was used yielded negative findings on 196 D-dimer assays, false nega-

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positive findings on 1 assay, and positive assays of which 27 patients had DVT confirmed by positive findings on CUS. We used these data to calculate sensitivity, negative predictive value, specificity, and positive predictive value. In addition, these four parameters helped us use a Bayesian statistical analysis that estimates the probability of a hypothesis when pretest odds and likelihood ratio are known values. This Bayesian analysis gives us a probability estimate for the presence of DVT when a patient presents with either a positive or a negative D-dimer assay.

The bioMérieux system yielded a sensitivity of 96.4%, a negative predictive value of 99.5%, a specificity of 41.3%, and a positive predictive value of 8.8%. Using a Bayesian analysis, we can estimate that after negative findings on a bioMérieux D-dimer assay, the probability of DVT will be 1.8%; we can estimate the probability after positive findings on a bioMérieux D-dimer assay to be 25%.

For the 512 patients for whom the Trinity Biotech test system was used, there were 316 negative results on D-dimer assays, 1 false negative result, and 195 positive results; 39 of those latter patients had DVT confirmed by positive results on CUS. We used these data to calculate sensitivity, negative predictive value, specificity, and positive predictive value. In addition, these four parameters helped us use a Bayesian statistical analysis that estimates the probability of a hypothesis when pretest odds and likelihood ratio are known values. This gave us a probability estimate for the presence of DVT when a patient presented with either positive or negative results on a D-dimer assay.

The Trinity Biotech system yielded a sensitivity of 97.5%, a negative predictive value of 99.7%, a specificity of 66.9%, and a positive predictive value of 20.0%. Using Bayesian analysis, we estimated the probability of DVT after negative findings on a Trinity Biotech D-dimer assay to be 0.8% and after positive findings to be 38%.

Discussion
The formation of DVT is normally followed by a physiologic fibrolytic response. As a result of this fibrolytic response, plasmin is generated, which causes the release of fibrin-degradation products into the circulation. Because D-dimer is the predominant form of fibrin-degradation product, the absence of a clinically significant rise in circulatory D-dimer implies that thrombosis is not occurring. This is why negative results on D-dimer assays have played such an important role in excluding the diagnosis of DVT. It is therefore most strategic to employ a D-dimer assay that has both a high sensitivity and a high negative predictive value. The specificity and positive predictive value have not been emphasized and have historically produced variable results. False positive results have become common when testing for D-dimer.

Our study compared two D-dimer methodologies, postulating that one of them, the Trinity Biotech immunoturbidimetric latex Auto-dimer immunoassay, would maintain a high sensitivity, an excellent negative predictive value, and Bayesian negative probability while greatly improving specificity, positive predictive value, and Bayesian positive probability. Improving specificity, positive predictive value, and Bayesian positive probability would also significantly decrease the number of false positive D-dimers and decrease unneeded usage of CUS.

Our study showed that with the Trinity Biotech D-dimer test methodology, all parameters for clinical performance improved, including sensitivity, negative predictive value, negative probability, specificity, positive predictive value, and positive probability (Table 1). Greatly significant for our study, when we used the Trinity Biotech D-dimer test, specificity increased from 41.3% to 66.9%, positive predictive value increased a statistically impressive 2.3 times from 8.8% to 20.0%, the Bayesian probability of DVT after positive results on a D-dimer test significantly increased 1.5 times from a 25% probability to a 38% probability, and the Bayesian probability of DVT decreased a statistically impressive 2.3 times from 1.8% probability to 0.8% probability (Table 1).

In addition to the improved parameters for clinical performance, a significant number of unneeded CUSs were saved. The number of false positive results for the bioMérieux system was 279/503; for the Trinity Biotech system, it was 156/512. This was a decrease of 123 unneeded CUSs over a six-month period. With the billable cost for each CUS being $315, and our cost per D-dimer test being the same for both the bioMérieux and the Trinity Biotech assays, we calculated that a potential six-month CUS savings of $38,745, or a more significant annual CUS savings of $77,490, could be realized by using the Trinity Biotech D-dimer assay.

Future investigations for D-dimer research might...
include examining a wider patient source, including inpatients and those suspected of having pulmonary embolism. Much work is still needed to improve the standardization for D-dimer assays, and newer technologies for assay methods that help establish clot age and the probability of DVT recurrence will require thorough assessment.

* Trinity Biotech, Wicklow, Ireland

**Acknowledgments**

Bill Paringer, Grace Johnston, Bovi Nielsen, and Leah Diaz (Kaiser Permanente Medical Library, Fontana, CA) provided outstanding research assistance for this study. Katharine O’Moore-Klopf, ELS, of KOK Edit provided editorial assistance.

**References**


**Keep Moving**

Perhaps the secret of avoiding blood clots lay in the humble admonition of the London bobby: “Keep moving!”

—Alastaire Cooke, KBE, 1908-2004, British-born American journalist and broadcaster
Introduction

Every profession spawns a dialect, a language that facilitates efficient communication among insiders. In written communication, that dialect often becomes even more compact, as acronyms and code words are substituted for “plain text.” This tendency has received some attention in the government sector (where efforts to translate bureaucratic jargon into English periodically gain media attention) but much less so in health care. Yet we may well have reached the point in health care at which the dialects spoken by practitioners and health policy experts are not just confusing to outsiders, but actually prevent us insiders from achieving our goals. The findings presented here emerged from what began as a qualitative marketing study, but which revealed a tremendous gap between what health care professionals say and what health care consumers hear.

That the unfettered use of our professional dialect may be counterproductive is highlighted as two recent health care trends collide: the ever-increasing complexity in the language of health care occurring at the same time that we are asking lay people—as patients, consumers, and voters—to take a more active role in their health and health care choices.

The language of health care and health policy has grown more complex over time as new diseases and conditions have been identified, new treatments discovered, and new ways of reimbursing providers implemented. Physicians who once could do little about heart attacks now treat “acute myocardial infarctions” with “beta blockers, angiotensin-converting enzyme inhibitors, and drug-eluting stents.” The Medicare program that once paid whatever numbers physicians wrote on their bills, now bases payments on “resource-based relative values” that are multiplied by a “geographic practice cost index” and a “conversion factor” and whose growth over time is determined by a “sustainable growth rate mechanism.”

Twenty, perhaps even ten years ago, the discrepancy between professional and lay dialects did not particularly matter. Just as one need not be an engineer to drive a car, patients did not need to understand medical jargon or health care policy. But that has changed. Increasingly, we want consumers to be “empowered,” and to take an active role in maintaining their health, not to be passive recipients of medical care. Consumer “choice” forces health care organizations to differentiate themselves, which they try to do by packaging and selling their new and improved services. We want voters to understand policy alternatives and assess options for change. Perhaps most importantly, we want to enlist patients and consumers to advocate for change in the way that health care is delivered and force the system to improve quality and efficiency.

American health care consumers do not speak our dialect, and they perceive and understand our health care system in a very different way. Patients have strong opinions about health care based on their individual health conditions and their experience with that part of the largely fragmented delivery system in which they receive care. The problem is that in trying to enlist these patients and consumers, the provider and policy communities have gone full speed ahead in developing new ideas without bothering to investigate whether those new ideas and the words used to describe them resonate with the audience. Professional journals, trade publications, and policy blogs are replete with terms such as evidence-based medicine, care coordination, health information technology, medical home, and comparative effectiveness. From an insider perspective, these terms all describe ideas intended to make our health care system better. But do they mean anything to consumers?

Before true health care reform can take place, we must convince patients that their needs will be fulfilled through whatever changes are made: at the national level to heal the ailing health care system,
and locally, in individual physicians' offices to heal ailing patients themselves. But how do we convince them that any new model of health care delivery will benefit them? What words will work?

Study Purpose

The Council of Accountable Physician Practices (CAPP), an affiliate of the American Medical Group Association, is a coalition of multispecialty medical groups and integrated health systems united in their commitment to coordinated, integrated health care. As part of its ongoing work to promote the benefits of this health care delivery model to consumers and media, CAPP created a marketing campaign that used a number of words and messages to describe care coordination. Before launching the campaign, CAPP realized that it needed to test key words and the messages that used these words to see if they would resonate with the average consumer.

CAPP hired a professional health care market research firm to assist in this effort. The firm recommended that the message testing take place through a series of focus groups, which, unlike survey research or other quantitative methods, allow for in-depth probing of respondents' attitudes and experiences. This qualitative research method would provide the flexibility CAPP needed to explore unanticipated issues and better understand consumer attitudes, which would not be possible within the more structured, and often inadvertently biased, questioning of survey questionnaires. The objective was to find out how the majority of Americans understand a particular word or phrase, but to understand what associations and connotations the term could have, and whether they were generally positive or negative.

The focus groups were charged with exploring three questions:

1. How do consumers think about quality health care? (In other words, what is it they think they need?)
2. How is the provider/policy health care lexicon understood?
3. What words and phrases can health care professionals use to reach consumers to promote the benefits and attributes of coordinated care and organized delivery systems?

Methodology

The study was composed of ten focus groups conducted between November 2007 and February 2008 in Boston, MA; Edina, (St Paul) MN; Billings, MT; San Diego, CA; and New York, NY. The focus groups were conducted during the week with English-speaking women. Women were targeted because it is generally accepted in health care marketing that they make the majority of health care purchasing decisions. Participants were segmented by age: (1) women, ages 35 to 54 years, often responsible for making health care choices for their families; and (2) older women, ages 55 to 70 years, who also make health care decisions for their families and who have an increased need for medical services. Except for New York City (which does not have a comparable organized delivery system from which to recruit patients), both CAPP patients and nonpatients were included in the study to account for varying levels of familiarity with coordinated care. Participants were screened to represent a mix of income levels around the median for their region of the country. All participants had, at a minimum, a high school education. The education and income levels were chosen because the final CAPP marketing campaigns would target this group as being most engaged in making health care decisions within the private or employer-sponsored health insurance system. (Not surprisingly, the New York participants were more highly educated and had a much higher median income than the other groups across the country.)

Twelve participants were randomly recruited for each group by a professional focus group firm in each city using databases from the research facility and from the participating local CAPP medical group. The first group was held at 6:00 in the evening and the second group was held at 8:00 in the evening. All groups were held at a focus group facility, equipped with a two-way mirror for viewing. The recruitment process resulted in 8 to 11 participants in 9 out of the 10 groups. Due to weather conditions on the night of the focus groups, only four participants attended the later group in Edina, MN. The number of participants in this group, although smaller than the standard focus group size, is sufficient for qualitative analysis from a market research perspective.

Participants received an incentive between $60 and $100, depending on the target market and expected show rates, and were served a light meal. Each focus group was audiorecorded and videotaped to provide an accurate account of the discussion. Each group lasted approximately two hours.

In each group, a professional facilitator led the participants through the following agenda:

1. A discussion about the participants' general attitudes about health care.
2. A rating of individual key words,
with a subsequent discussion of each, which included the participants trying to use the words in a health care context.

3. A review of marketing materials: During this section, the focus group was asked to react to specific taglines, descriptions, and marketing materials developed for CAPP that used some of the terminology that was rated. Since these marketing materials are proprietary, the results of that part of the focus group are not presented in this report.

The sponsor of the study (CAPP) was identified at the start of each group to engender trust and foster open, honest communication among the participants. There was little awareness of CAPP among the participants because CAPP had not yet marketed to or communicated directly with consumers, so there was no bias to consider in the evaluation of the results. The names of the participants’ individual physicians or medical groups, however, were not revealed by the focus group facilitator.

Results: General Consumer Attitudes About Health Care

To provide a framework for participants’ views on specific aspects of health care, the focus groups began with open-ended discussion around three questions:

• What factors did you consider in selecting your current physician or medical group?
• How do you feel about the quality of medical care you and your family are currently receiving?
• How do you define quality health care?

Not surprisingly, patients select their personal physician on the basis of recommendations from friends and family. Perhaps in part because participants lack information, they pay less attention to the medical group itself, usually selecting one from among the limited options offered through their employer-sponsored health plan. The most frequently cited factors in choosing a group were cost and location.

Participants’ views of quality varied. Only a few participants talked about technical expertise, medical training, or familiarity with current research and treatment options when discussing the quality of medical care they receive from their physician. And whereas some in each group remarked on the importance of convenience—including location, hours, wait time, after-hours care, and care coordination—it was clear that the primary driver of satisfaction is the physician/patient relationship. Patients seek physicians who “listen,” “care,” and provide “personalized” services; they attributed poor medical care—such as misdiagnosis or incorrect treatment—to physicians who are “rushed” or fail to listen.

“The doctor rushed us in and rushed us out. The diagnosis was wrong because he didn’t listen.” —Boston participant.

“Quality health care is when you leave the doctor’s office and your questions have been answered … when I leave I feel satisfied that we made the right decision [regarding care]. They explain everything.” —Edina participant.

Attitudes toward care were similar across geographic regions, but there were significant differences by patient status, age, and health. For example:

• Participants currently receiving coordinated health care services, and those experiencing health problems, were more likely than other participants to give examples of care coordination when asked how they selected their medical group and how they defined quality care.
• Younger women, age 35 to 54 years, particularly working mothers, placed greater importance on convenience than did older women.
• Older women, age 55 to 70 years, placed the greatest emphasis on the physician’s bedside manner and the level of personalized care.
• Older women were least likely to embrace the use of e-mail and electronic medical records. Such technology, they felt, was impersonal and interfered with direct communication between physician and patient. (Those whose physician had explained the importance of computerized records were more supportive of technology.)

One significant regional difference we did find was that New Yorkers were more willing than lower- and middle-income consumers in the CAPP markets to question their physician’s expertise and were more willing to switch physicians if their expectations were not met. As one New York participant explained, “I think that basically you have to take care of yourself. If it doesn’t smell right, get out.” New Yorkers did value their personal relationship with their physician, but they also placed more emphasis on their physician’s training and familiarity with the range of treatment options than did other consumers. “The things that matter to me are: the expertise that the doctor has had and the frequency with which the doctor has performed a procedure,” said one participant.

Regardless of age, health, or type of medical group/delivery system
From Our Lips To Whose Ears? Consumer Reaction to Our Current Health Care Dialect

The majority of participants evaluate the quality of their medical care primarily in terms of their personal relationship with their physician. What patients primarily believe they need is not better quality care (or a delivery system that can deliver it), but a physician they can trust. The challenge for proponents of delivery system reform is to find language and messages that do not force patients to question their beloved physician’s expertise, but do make them more aware of what quality care should be and how it should be delivered.

**Results: Word Associations**

Focus group participants were then asked to score key words on a scale of one to four, where one is negative and four is positive. After they rated the terms, the facilitator asked the respondents to comment on their ratings. During this time, the participants were encouraged to talk about the words and try to use the terms in context. Participants often assisted each other to try to better understand what the words meant. These rating procedures were designed to enrich the discussion and do not represent a statistical sample of consumers; therefore, the rating scores are not presented in this report as percentages or counts. Instead, the score results have been combined with the researchers’ qualitative analysis of the participants’ subsequent discussions to draw conclusions.

The following terms were tested:
- Integrated care
- Coordinated care
- Medical home
- Multispecialty medical group
- Integrated health care delivery system
- Medical decision support
- Evidence-based medicine
- Best practices
- Accountable

**Negative Terms**

**Medical Home**

“Medical home,” coined by the American Academy of Pediatrics and recently further defined by the American Academy of Family Physicians, is a term that has quickly been adopted by health plans, policymakers, and politicians (including the 2008 presidential candidates). Our findings suggest it is unlikely that the term was tested with consumers, however, because it consistently received the lowest scores among all the terms tested. Participants associated “medical home” with nursing homes and end-of-life care, with only a few thinking it described coordination of medical services through a primary care physician or group.

“It just sounds like a nursing home.” —Boston participant.

“First you go to the medical home and then you go to the funeral home.”

### Table 1. Most negative terms

<table>
<thead>
<tr>
<th>Word</th>
<th>Negative association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical home</td>
<td>Nursing home, home health, end of life</td>
</tr>
<tr>
<td>Medical decision support</td>
<td>End-of-life decisions</td>
</tr>
<tr>
<td>Guidelines or treatment guidelines</td>
<td>Restrictive, rigid, limited, driven by cost</td>
</tr>
<tr>
<td>Integrated health care delivery system</td>
<td>Bureaucratic, industry language, meaning unclear</td>
</tr>
<tr>
<td>Integrated care</td>
<td>Bureaucratic, industry language, meaning unclear</td>
</tr>
<tr>
<td>Multispecialty medical group</td>
<td>Bureaucratic, industry language, meaning unclear, trying to do too much, low quality, limited choice of specialists to choose from</td>
</tr>
<tr>
<td>Best practices</td>
<td>Bureaucratic, meaning unclear, insincere, cookie-cutter care, not tailored to the individual</td>
</tr>
<tr>
<td>Evidence-based medicine</td>
<td>Impersonal, one size fits all</td>
</tr>
<tr>
<td>Accountable</td>
<td>Something will go wrong, minimal care, buzz word</td>
</tr>
</tbody>
</table>

### Table 2. Most negative terms—New York City

<table>
<thead>
<tr>
<th>Word</th>
<th>Negative association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical home</td>
<td>Nursing home, home health, end of life</td>
</tr>
<tr>
<td>Medical decision support</td>
<td>End-of-life decisions</td>
</tr>
<tr>
<td>Care protocols</td>
<td>Restrictive, one size fits all</td>
</tr>
<tr>
<td>Multispecialty medical group</td>
<td>Limited choice of specialists to choose from, forced to choose within group instead of getting the “best”</td>
</tr>
<tr>
<td>Best practices</td>
<td>Bureaucratic, insincere, cookie-cutter care, not tailored to individual, legal disclaimer</td>
</tr>
</tbody>
</table>
medical care. Only a few in each group found the word positive and reassuring. By contrast, New Yorkers gave “evidence-based medicine” mixed results. Some found the term confusing and wordy. Participants who had heard the term used in their own professions found it positive, associating it with lower-quality care. Participants not familiar with the term or found it to be a catchphrase: “overused,” “bureaucratic,” and “insincere.” Some associated “best practices” with limitations on what care a patient could receive.

“Evidence based on what? The pharmaceutical company that ran the test so their medicine would be favored?” —New York participant.

“I thought [evidence-based medicine] was silly. If medicine isn’t based on evidence what is it based on?” —New York participant.

“You hope that the research has been done.” —New York participant.

Evidence-Based Medicine

Except for New Yorkers, participants were very skeptical of this term. They believed it to be a “one-size-fits-all” approach that would undermine personalized medical care. Only a few in each group found the word positive and reassuring. By contrast, New Yorkers gave “evidence-based medicine” mixed results. Some found the term confusing and wordy. Participants who had heard the term used in their own professions found it positive, associating it with lower-quality care. Participants not familiar with the term or found it to be a catchphrase: “overused,” “bureaucratic,” and “insincere.” Some associated “best practices” with limitations on what care a patient could receive.

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“I thought [evidence-based medicine] was silly. If medicine isn’t based on evidence what is it based on?” —New York participant.

“You hope that the research has been done.” —New York participant.
of accountability as a defensive position used to prove that a physician or organization has not violated professional standards, an indicator of minimal care. Consumers expect their physicians and medical groups to be “accountable,” seeing the term raises their concerns. Some liked the term, interpreting it to mean that they will get good, responsible care. “They are communicating a standard.” Several reported that they thought the term was overused. “I get a middle-of-the-road feeling. I hear it so much in politics. ‘He has to be held accountable for this or else.’”—San Diego participant.

“I think it is kind of scary. It is telling me … I am going to go there and something bad is going to happen and someone has to be held accountable for it.”—San Diego participant.

“I would think that this would be a totally unnecessary word.”—San Diego participant.

Positive Terms
Of the top three most positive terms from both sets of focus groups, only two were ranked unambiguously positive by both the general focus group participants (Table 3) and the more highly educated New Yorkers (Table 4): communication and coordinate/coordinated care.

Communication
The term “communication” received the highest rating of any words tested across all groups. Participants interpreted communication to mean communication between physicians and patients, but also between physicians and their medical staff. Communication was associated with physicians who listen and answer patients’ questions.

“Communication means getting answers to your questions.”—Edina participant.

Treatment
“Treatment” was a positive term for both patients who interpreted it as a reference to medical practice and those who interpreted it as a reference to customer service. A few people negatively associated treatment with serious illness, although this was a minority opinion.

“You are going to get better.”—Edina participant.

“It’s the emotional treatment.”—Boston participant.

Coordinate/Coordinated Care
Participants associated the verb “coordinate” with efficiency and communication; they viewed “coordinated care” as less sincere, more bureaucratic, and less clear. This was particularly true for patients of less organized delivery systems, who were probably less familiar with the term.

“Sounds like people taking care of everything for you.”—Boston participant.

“Putting all of the pieces together to make the whole.”—Billings participant.

Integrated care
This term tested more positively among New York participants than among other consumers. Most New Yorkers understood the term to mean commitment, teamwork, and coordinated care. A few associated the term with industry language that was deliberately ambiguous.

“[Integrated care] is working together … and coming up with a solution.”—New York participant.

“[Integrated care] is five different types of doctors working together … if the person has five different problems.”—New York participant.

Terms with Mixed Results
A number of terms were not ranked particularly high or low, but the participants’ interpretations are intriguing (Tables 5 and 6).

Value
The term “value” received mixed results. Rating it highly were those who interpreted it to mean that they (as patients) were valuable. Participants who heard “value” to mean cost effectiveness or low cost gave the term low scores. To avoid misinterpretation, discussions of value in health care should combine

<table>
<thead>
<tr>
<th>Table 3. Most positive terms</th>
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<tbody>
<tr>
<td>Word</td>
</tr>
<tr>
<td>Communication</td>
</tr>
<tr>
<td>Treatment</td>
</tr>
<tr>
<td>Coordinate</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4. Most positive terms—New York City</th>
</tr>
</thead>
<tbody>
<tr>
<td>Word</td>
</tr>
<tr>
<td>Communication</td>
</tr>
<tr>
<td>Coordinated care</td>
</tr>
<tr>
<td>Integrated care</td>
</tr>
</tbody>
</table>
From Our Lips To Whose Ears? Consumer Reaction to Our Current Health Care Dialect

messages about quality.

“I was thinking that I was of value and worth the time the doctor’s going to spend.” —Boston participant.

“It reminded me of buying a shirt … I don’t rate a doctor in terms of whether she’s a good value for my dollar.” —Boston participant.

“It means things are cost effective. They are going to keep the value down. You aren’t getting the best care.” —Edina participant.

Teamwork

“Teamwork” did not resonate with participants, many of whom commented that the word reminded them of business terminology and sports. Participants liked the idea of people working together and associated the concept with increased communication, but ultimately found the term to be “fluffy” and overused. Interestingly, a few participants expressed concern that teamwork implied that there was no “captain,” someone taking responsibility for coordinating services.

“It’s nice, but I don’t have strong feelings.” —Edina participant.

“I don’t have any bad connotations of the word. It just didn’t tell me anything.” —Edina participant.

Convenient Care

The mixed results given “convenient care” illustrate the subtleties at play. Although participants—particularly younger women with children—desire convenience, they associate the promotion of convenience with poor medical care. Convenience was associated with urgent care, “sloppy services,” and convenience stores or fast food eateries. People who liked the term, however, associated it with minimal waiting times, multiple locations, and extended hours. As with “value,” the term “convenient care” should be coupled with messages about the delivery of quality care.

“Convenient care does not always seem like the best.” —Boston participant.

Treatment Guidelines

Some participants liked the term, associating guidelines with quality control and medical standards, while others felt it implied restrictions to medical treatment. “If you have a heart problem this is how we are probably going to treat it … this is the correct way of going about it,” said one participant. However, other participants felt differently, as expressed by one woman, “[Treatment guidelines mean] I can only give you six injections. If you need eight, too bad.”

“You don’t want to be put into a slot—According to our guidelines, this is all we can offer you.” —San Diego participant.

Discussion

The limitations of a qualitative study involving only a hundred or so participants in a few select markets notwithstanding, three key findings emerged that have some profound implications for health care practitioners and policy makers.

First, consumers think differently about quality than do health care professionals. For them, quality care is entirely about the relationship with their physician. Even when asked to define quality specifically, not one participant referenced clinical quality; they referenced only their comfort and trust in their physician. From these discussions, we could not tell whether participants were unaware of the extensive literature on health care quality (most likely) or knew of the literature but did not value it highly. What is clear is that the slide on quality and errors that appears in every presentation on health care reform is asserting the need to fix a problem that these consumers were not aware existed.

Second, our professional language is not well understood by patients, an unsurprising result. More surprising was the variability in reactions. In some cases, participants’ views of particular terms may be dominated by their experi-
From Our Lips To Whose Ears? Consumer Reaction to Our Current Health Care Dialect

The consumer is bombarded by messages about all kinds of services and products through multiple channels on a daily basis. Consumer interpretations of words like “teamwork,” “value,” “convenience,” etc., are informed by life experiences, not just health care experiences (so that “value” connotes 99 cent hamburgers). In other cases, professional buzz-words do not resonate because consumers’ expectations are so different. For example, participants had no clue what evidence-based medicine meant and when told, asked “What else would physicians use?” Whereas Washington, DC is abuzz with efforts to put science back in medicine, these consumers did not know it had ever left.

The different reactions of participants in New York City are a reminder that national discussions of policy must proceed mindful that health care is a very local concept, both in terms of its delivery and its context. For example, living in a city famous for both its academic medical centers and its “anything you want, 24/7” consumer culture gives New Yorkers a different way of thinking about and talking about health care. We must understand that not only will the health care “solution” vary geographically, but so must the way we talk about it.

Finally, how should we think about reaching consumers? First, be aware that even seemingly neutral or positive words may have very different connotations. The term “medical home,” for example, a favored concept among experts for promoting care coordination, conjured up images of nursing homes and “places where you go to die.” Participants associated “treatment guidelines” not with helping physicians navigate a complex world to make better care decisions, but with limiting what physicians can do. Even the word “delivery” was viewed negatively, making medicine sound like a package or letter!

As we try to convey the benefits of our system, we need to remember that any new process, tool, innovation, service or feature that is being rolled out to patients should be positioned as being a support—and not a hindrance—to emphasize the improved communication that will take place between the clinician, the patient, and the medical staff. Each patient likes to know that his/her clinicians are conferring together and communicating on his/her behalf.

- Although clinicians understand the benefit of evidence-based medicine and treatment guidelines, consumers can associate these terms with cookie-cutter treatment and an attempt to override their physician’s best judgment. If you feel the need to explain evidence-based treatments and guidelines (using these terms), do so by telling your patient how these protocols assist you in making better judgments, and that you would not advise such treatment if you had not already considered their very particular case. In other words, personalize.

- The benefits of care coordination and system integration are not well understood by the consumer. Physicians can do much to educate their patients about what they should look for in quality care and medical services by speaking positively about the support services you and your patients have. If, for example, your patient has a chronic condition that requires education, follow-up, and oversight by several care providers, describe how this team approach will benefit the patient with you, the physician, at the helm, following the patient’s case and monitoring their progress.

- Speak to your patients simply and straightforwardly. Complex medical terms can be anxiety provoking and industry terms can feel bureaucratic and impersonal. Consumers seek a strong personal relationship with their physician, which comes from trust. Trust is engendered through clear communication—understanding and being understood.

Implications for the Practicing Physician

These focus group results highlight yet again the primacy and importance of the physician-patient relationship. The physician holds the unique position of being the major influence on a patient’s understanding of health care and their decision making, a fact that pharmaceutical and other companies selling health care products understand very well. Our own organizations fail to take full advantage of the physician “sweet spot” in communicating with patients, and many physicians themselves don’t understand the strong effect that their language and communication skills have on their patients.

Organized delivery systems and medical groups that invest significant time and money on developing new care processes and support services for patients should be aware of the consumer reaction to the health care terminology we tested in this study. Practicing physicians can also do much to support their organizations and promote aspects of quality care by paying more attention to their own language use. Here are a few tips that emerged from this study:

- When talking to patients about a new service or feature (such as after-hours care, specialist referrals, in-house medical services), emphasize quality care over convenience or cost. Although consumers want and need convenient and cost-effective medical care, they associate these terms with low-quality, minimal, and impersonal care. If your organization has put a process or service in place to make care delivery more “convenient” for patients, promote that feature as a component of “top drawer” service.
- When talking about the benefits of a new feature—such as an electronic medical record or new physician-patient e-mail capability—
the physician-patient relationship. In other words, our language should describe how the new feature will help address the patient’s core need—to continue to trust the personal, caring relationship that exists between physician and patient. (See sidebar: Implications for the Practicing Physician.)

Taken together, these findings suggest that, at a minimum, engaging consumers requires thinking more carefully about the language we use and, perhaps, behaving a little more like marketers and doing some pretesting. How can we ever hope to influence our most important constituents if they do not understand one word we say?

There is a more profound issue here as well, namely that all of us have a difficult time conceiving of a world significantly different than the one in which we live. Our New York City participants, for example, discussed the need to bring all their medical files to every appointment. The notion that an integrated delivery system with an electronic medical record—much less a Web-based system that aggregated information across independent providers—might routinely have all of the relevant information was not in their imagination. Solutions to problems people don’t know they have won’t be easy to sell.

Finally, this investigation not only provided the CAPP team with valuable feedback on our specific marketing messages, but highlighted the fact that wide communication gaps exist in our industry that beg for further detailed investigation and study.

Disclosure Statement
This study was commissioned by the Council of Accountable Physician Practices, an affiliate of the American Medical Group Association and partially funded by the Kaiser Permanente Institute for Health Policy, which also provided input into the questionnaire design. Dr Ross is a Vice President of the Kaiser Foundation Health Plan, Inc and the Director of Kaiser Permanente Institute for Health Policy, and Ms Igus and Ms Gomez are both consultants to the Council of Accountable Physician Practices.

References

The Same Language

Ever since I told a crowded room I had a Bavarian cyst and not only did no one laugh, but two others had the same thing, I’ve been convinced that doctor and patient do not speak the same language. They speak Latin. We speak Reader’s Digest.

—Erma Bombeck, 1927-1996, American humorist and newspaper columnist
"Thrive"

16 x 20"
Oil on canvas

By Samir Johna, MD, FACS

Dr Johna is an Associate Clinical Professor of Surgery at Loma Linda University School of Medicine in Loma Linda, CA. He is a Staff Surgeon at the Fontana Medical Center in Fontana, CA.
Blood-Management Programs: A Clinical and Administrative Model with Program Implementation Strategies

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Jose Almeda, MD
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Jennifer Kim
Randy Henderson
Mitra Nadim, MD
Linda Sher, MD
Robert R Selby, MD

Jehovah's Witnesses and the Historical Evolution of Blood Conservation

Everything that lives and moves will be food for you. … But you must not eat meat that has its lifeblood still in it. For your lifeblood I will surely demand an accounting.

—Genesis 9:3–5, Old Testament, New International Version

Any Israelite or any alien living among them who eats any blood—I will set my face against that person who eats blood and will cut him off from his people. For the life of a creature is in the blood, and I have given it to you to make atonement for yourselves on the altar; it is the blood that makes atonement for one’s life. Therefore I say to the Israelites, “None of you may eat blood, nor may an alien living among you eat blood.”

—Leviticus 17:10, 12, Old Testament, New International

You must abstain from eating food offered to idols, from consuming blood or the meat of strangled animals, and from sexual immorality.”


Jehovah’s Witnesses is a religious organization whose adherents now number more than six million worldwide. The sect was established in 1870 in an effort to return to a pure, unadulterated, scripture-based form of Christianity; consequently, many of the group’s doctrines are derived from literal interpretations of the Bible. Though best known for its evangelical efforts, the organization has gained notoriety for its controversial stance on blood transfusions, which its adherents believe to be a violation of God’s law. To them, the “life force” resides in the blood, and oral or intravenous ingestion can result in the forfeiture of eternal life and excommunication from the congregation. Because of their beliefs, Jehovah’s Witnesses faced resistance and criticism from the medical community. Fearful of undergoing transfusion against their will or without their knowledge and unable to find hospitals willing to treat them in accordance to their religious precepts, members would, at times, risk their health and well-being to avoid medical intervention. The first bloodless surgery program was developed for this population. By coordinating presurgery counseling, specialized equipment, and physicians trained in perioperative and postoperative nonblood therapies for the prevention and treatment of anemia, blood-management programs ensure that patients can access treatment without having to forfeit their beliefs.

The first bloodless surgery program was established to offer Jehovah’s Witnesses access to medical treatment in an environment that coincided with their religious belief system. It and other similar programs were designed to be transfusion-free, using a method of blood management that strictly disallows the administration of allogenic cellular transfusions (red blood cells [RBCs], white blood cells, platelets), as well as many serum protein products, despite the risk of patient mortality. The importance of...
Blood-Management Programs: A Clinical and Administrative Model with Program Implementation Strategies

Table 1. Additional charges in US dollars to patient: US cost of blood transfusion

<table>
<thead>
<tr>
<th>Component</th>
<th>Cost/unit ($)</th>
<th>Service fee ($)</th>
<th>Subtotal ($)</th>
<th>Units/year</th>
<th>Total ($)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Red blood cells</td>
<td>276</td>
<td>728</td>
<td>1004</td>
<td>14,000,000</td>
<td>14,066,000,000</td>
</tr>
<tr>
<td>Platelets</td>
<td>500</td>
<td>200</td>
<td>700</td>
<td>1,400,000</td>
<td>980,000,000</td>
</tr>
<tr>
<td>Cryoprecipitation, fresh frozen plasma</td>
<td>50</td>
<td>250</td>
<td>300</td>
<td>13,600,000</td>
<td>4,080,000,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td><strong>2004</strong></td>
<td></td>
<td><strong>19,126,000,000</strong></td>
</tr>
</tbody>
</table>

maintaining a transfusion-free environment requires the hospital to implement comprehensive preoperative, intraoperative, and postoperative safety measures as well as patient tracking systems to prevent inadvertent blood product administration to this specific patient population. Ultimately, the program demands a degree of institutional commitment with administrative and operational precision that many hospitals are unable to provide.

Blood-management programs have since advanced to lie on a spectrum from transfusion-free practice to less restrictive alternatives based in a common effort to minimize blood product administration. Their development, which began as an alternative for those with religious beliefs that prohibit the acceptance of blood products, is also driven by the concept that minimizing blood product administration enhances patient safety and reduces the cost and length of hospital stays. Using many of the same clinical strategies to avoid blood product administration, a blood-conservation program can avoid problems with the availability and escalating costs of blood products and take advantage of the fewer complications and increased patient safety associated with decreased allogenic transfusion. In addition, hospitals that are unable to provide transfusion-free programs still have the opportunity to take advantage of the financial and clinical benefits of a blood-management program without the bureaucratic complexities of unconditional prohibition of cellular transfusion that a transfusion-free program would require.

**Transfusion—At What Cost?**

There is a significant financial cost associated with blood products, generated by the process of collecting blood donations, processing and testing specimens, storage, and transfusion.

Once blood products arrive at a hospital blood bank, other charges are levied: typing ABO; typing Rh; antibody screen; cross-match, immediate spin; cross-match, antiglobulin (Coombs phase); red blood cell antigen screening (per antigen); fresh frozen plasma thawing; cryoprecipitate pooling; and antigen phenotyping.

In addition, transportation, handling, and waste management require hospitals to affix additional charges that in the end, can multiply by fivefold the cost of the blood product itself (Table 1).

The cost of a single unit of blood has quadrupled since the late 1980s, and when the potential cost of adverse events and increased hospital stay is added, the financial burden is immense. Shander uses this “cost-of-blood equation” to estimate the cost of transfusion (Figure 1).

What this rather complex mathematical equation depicts is how the cost of transfusing ($C_{tot}$) is actually the sum of the individual costs incurred at each step, multiplied by the number of times that each step was repeated. Shander identifies nine important steps: donor cost, production, hospital transfusion preparation, administration of blood products, treatment of adverse outcomes, treatment of transfusion-related disease, litigation, lost productivity, and organization of nationwide hemovigilance systems. What this demonstrates, most importantly, is a global picture of how a single transfusion can incur seemingly unrelated costs.

Many of these extra costs can be controlled through the implementation of a blood-management program. Englewood Hospital in Englewood, New Jersey instituted a blood-saving program through which it has decreased RBC transfusions by 20% since 1994. Staff were able to decrease operating room (OR) transfusions to constitute only 5% of total transfusions in 1998, down from 50% in 1994. Instituting such an effort translated into direct financial return. Interestingly, those patients in the blood-conservation program saved even more resources than those who ultimately did not even need a transfusion, illustrating the cost of transfusion even when transfusion is not performed.

Financial burden, although significant, is not the most important cost of allogenic blood-product transfusion. There is an inherent risk of morbidity and even mortality associated with the transfusion of blood products, the safety and efficacy of which rely on the integrity of the blood product as well as the transfusion process itself.

Although transfusion reactions are rare, a small percentage of blood-product recipients experience adverse effects that can be severe. The risk of infection, even if small, is still an important consideration, with transmission of viruses, bacteria, and parasites all possible.
Transfusion reactions range from benign to deadly, with various outcomes and frequencies (Tables 2 and 3).  

The cost of allogenic blood-product transfusion can be significant for patients with cancer, who have been shown to experience a higher rate of recurrence of their cancer than those who do not receive allogenic blood. Although the relationship between blood transfusion and cancer recurrence is still open to debate, several studies have shown that blood transfusion is a significant independent prognostic factor for cancer recurrence. Tarttar found, in one such study, that 40% of 110 patients who received transfusions developed cancer recurrence, compared with 22% of patients who did not receive blood, and that those who did develop recurrence received an average of twice as much blood as patients without recurrence. Makino et al found that perioperative blood transfusion enhances the risk of intrahepatic recurrence of hepatocellular carcinoma in patients with portal vein invasion. Although the relationship is still controversial and confounding factors are numerous, it has been documented that blood transfusion causes a complex immunomodulatory reaction that can include immunosuppression and cancer recurrence predisposition.

Furthermore, it has been documented that transfusion can increase risk of infection. One study documented that transfusion of > 4 U of blood increased the risk of perioperative infection by a factor of 9.28. A meta-analysis of 20 articles published between 1986 and 2000, reporting on studies of a total of 13,152 patients (5215 in a transfusion group and 7937 in a nontransfusion group), concluded that blood transfusion is associated with a significantly increased risk of postoperative bacterial infection, while taking into account confounding variables such as age, shock, and wound contamination.

All this potential morbidity adds to the financial burden of blood product administration, as the tests and procedures required for the proper diagnosis and treatment of these adverse effects add a hidden cost to both hospital and patient.

**Background: Anemia, Transfusion Safety, and Surgery Mortality**

Carson et al described a multicenter, retrospective analysis from 1981–1994 that reviewed treatment of 1958 Jehovah’s Witnesses patients (older than age 18 years) who declined transfusion, analyzing the effect of anemia and cardiovascular disease (defined as history of angina, myocardial infarction [MI], congestive heart failure [CHF], or peripheral vascular disease) and surgery mortality. The primary outcome was 30-day mortality, with a secondary outcome of 30-day morbidity in the hospital. Mortality rate was 11% in patients with a preoperative hemoglobin level of <10 g/dL, compared with 1.3% in patients with a hemoglobin level of >12 g/dL. Mortality increased linearly to 33.3% with a hemoglobin <6 g/dL. Arhythmias, respiratory failure, and CHF were the most common complications. These findings establish that overall mortality increases as hemoglobin level decreases and that even mild anemia is associated with some risk of death. This is supported by the findings of another study that showed an inverse correlation between preoperative hemoglobin levels and surgery mortality in surgery patients. A preoperative hemoglobin concentration of <8 mg/dL was associated with a 16.2% increased mortality rate, compared with patients who did not have anemia preoperatively.

These studies emphasize the danger in not transfusing Jehovah’s Witnesses patients in the setting of surgery. Although an attempt can be made to optimize their medical condition and improve their hematocrit levels with treatments such as iron or erythropoietin, these and similar interventions often take time that surgery patients do not have. Going into surgery with anemia that has not been properly addressed is often a reality for patients like Jehovah’s Witnesses who refuse transfusions, which places them at a severely increased risk of mortality.

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**Table 2. Frequency of viral infection**

<table>
<thead>
<tr>
<th>Virus</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytomegalovirus</td>
<td>3–12:100</td>
</tr>
<tr>
<td>Hepatitis B virus</td>
<td>1:63,000</td>
</tr>
<tr>
<td>Hepatitis C virus</td>
<td>1:103,000</td>
</tr>
<tr>
<td>Human T-cell lymphoma/leukemia virus</td>
<td>1:640,000</td>
</tr>
<tr>
<td>Human immunodeficiency virus-1</td>
<td>1:493,000</td>
</tr>
</tbody>
</table>

**Table 3. Frequency of hematologic reactions**

<table>
<thead>
<tr>
<th>Hematologic reactions</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hemolytic reactions</td>
<td>1:250,000 to 1:1,000,000,000</td>
</tr>
<tr>
<td>Delayed hemolytic reactions</td>
<td>1:1000</td>
</tr>
<tr>
<td>Transfusion-related lung injury</td>
<td>1:5000</td>
</tr>
</tbody>
</table>

---

Formula:

\[
C_{\text{txn}} = \left( c_1 x_1 + c_2 x_2 + c_3 x_3 + c_4 x_4 + c_5 x_5 + c_6 x_6 + c_7 x_7 + c_8 x_8 + c_9 x_9 \right) \div x_3 = \sum_{n=1}^{9} c_n x_n
\]

Figure 1. Shander’s cost-of-blood equation.  

blood management programs: a clinical and administrative model with program implementation strategies

in addition, anh blood can be reinfused at the same rate as any other transfused blood product and, if needed urgently, it can be reinfused via rapid transfuser. the volume of blood withdrawn for anh ranges between 400 and 1500 mL, depending on anticipated blood losses, original hemoglobin level, and patient tolerance; intravascular euveolemia is maintained with 5% albumin and crystalloid, whereas patient heart rate, blood pressure, pulmonary artery pressure, central venous pressure, and blood gases are continuously monitored. intraoperative transesophageal echocardiography can also be used to monitor cardiac contractility and ventricular filling. in our practice, the lowest hematocrit after anh was 21%; coagulation profiles were tracked by thromboelastogram, and approved components (factor vila, antifibinolitics, or protamine) were added as indicated for therapy.

anh has few contraindications, which include coronary heart disease, significant anemia, and pulmonary hypertension. it successfully creates a state of physiologic anemia that is well tolerated by most patients and generates a cushion against blood loss. reinfused whole-blood product produced by anh provides a barrier to hemorrhagic shock and ensures the safety of the patient during a state of predictable blood loss. it effectively lowers the risk of complications of autologous transfusions, including transmission of unknown pathogens, metabolic derangements, and citrate toxicity. it preserves blood bank resources and consequently reduces overall procedure cost (see table 4 for comparison between autologous blood donation and acute normovolemic hemodilution).

alternatives to allogenic blood-product transfusion: acute normovolemic hemodilution

currently, blood-product avoidance during surgery is centered on the understanding of blood and coagulation systems in surgery patients. acute normovolemic hemodilution (anh) is a broad therapeutic initiative that uses these principles of surgical blood systems to accomplish simultaneous removal of the patient’s blood and its replacement with a nonblood product.

the protocol for anh involves the removal of blood from a central line via gravity flow to a citrate phosphate dextrose adenine (cpda) bag, which remains in continuity with the patient and can be stored for up to six hours at room temperature (to best preserve platelet function) before being placed in a blood cooler for storage at 4° to 6° c. because the cpda tube and bag remain in continuity with the patient, the procedure conforms to the religious beliefs of jehovah’s witnesses. in addition, anh blood remains in the or and thus is not required to be registered in accordance with blood banking and storage regulations.

Furthermore, because of the dramatic increase in mortality, surgeons may choose not to operate altogether, putting these patients at an even greater disadvantage.

hebert et al determined that a restrictive strategy of blood transfusion is at least as effective as, and possibly superior, to a liberal transfusion strategy in critically ill patients, with possible exception of patients with acute mi and unstable angina. a total of 838 critically ill patients with euveolemia after initial treatment with hemoglobin levels of <9 g/dl were randomized into two groups, one in which a restrictive transfusion strategy was implemented and one in which a liberal strategy was used. the restrictive strategy implemented rbc transfusion at hemoglobin levels of <7 g/dl, and patients’ hemoglobin levels were maintained at 7.0 to 9.0 g/dl. the liberal strategy implemented transfusion at <10 g/dl, and patients’ hemoglobin was maintained at 10.0 to 12.0 g/dl. the researchers found that 30-day mortality was similar in the two groups, and with the exception of patients with significant cardiac disease, mortality rates were 6% lower (22.3% vs 28.1%) in patients where the restrictive strategy to blood transfusion was implemented, suggesting that not transfusing may be superior to transfusion in many cases. in addition, carson et al concluded that postoperative infections after allogenic transfusions were associated with a 35% increase in risk of serious bacterial infection and a 52% increased risk of pneumonia.

physiology and safety of acute isovolemic anemia

weiskopf et al described the human response to acute isovolemic anemia in a study of more than 21 volunteers, including 11 patients who were healthy before going under anesthesia. hemoglobin decreased from 13.1 g/dl to 5 g/dl, with critical oxygen delivery assessed with oxygen consumption, plasma lactate levels, and st changes on electrocardiographs. the hemodynamic responses to acute isovolemic anemia are shown in figures 2 through 5.

anh decreased systemic vascular resistance and oxygen delivery while increasing heart rate, stroke volume, and cardiac index. oxygen consumption increased slightly (from 3.07 ± 0.44 ml o₂ per kg/min to 3.42 ± 0.54 ml o₂ per kg/min) and plasma lactate levels did not change. anh to hemoglobin levels of 5 mg/dl in conscious healthy resting humans did not produce any inadequate systemic oxygenation. table 5 summarizes

acute normovolemic hemodilution... accomplishes simultaneous removal of the patient’s blood and its replacement with a nonblood product.
our own experience with acute normovolemic hemodilution in liver resection patients, and emphasizes its potential safety and efficacy.

The safe lower limit of hematocrit continues to be debated; however, the degree to which ANH is used can be titrated on an individual basis based on patient tolerance. Lower hematocrit levels during surgery may require additional cardiovascular monitoring to assess its impact on systemic functioning; persistent tachycardia and electrocardiographic changes suggestive of MI are usually the first signs of inadequate oxygen delivery as a result of anemia. Although ANH is contraindicated in certain patient populations, it can be expected that factors such as age, conditioning, and various comorbidities can limit the degree to which ANH can be tolerated; this has not yet been well established, and further studies are needed to address this matter.

A Comprehensive Approach

It would be imprudent to rely on a single drug or sole procedure to preclude transfusion. Rather, a comprehensive approach to blood conservation should be employed. Before surgery, erythropoietin, iron, and/or folate, can be used to increase preoperative RBC mass, a process labeled blood augmentation. ANH can be used in conjunction with intraoperative cell salvage (ICS), a technique that involves collection, washing, and reinfusion of the blood lost during surgery. Although ICS is an effective method for collecting blood from the surgical field, unfortunately, it salvages only the RBCs and not the associated clotting factors or platelets. Used in combination with ANH, which preserves the integrity of both the RBCs and clotting factors, the availability of a significant amount of safe, fresh, autologous blood can be ensured. Surgical skill, appropriate use of cautery, and meticulous technique can be used to combat excessive blood loss in patients. Preoperative and postoperative restriction of blood testing can also effectively minimize blood loss. Elimination of unnecessary laboratory tests, avoiding draws from the central line, and the use of pediatric tubes when blood draws are necessary can limit intensive care unit (ICU) blood draws to 40 mL to 75 mL of blood daily. Blood conservation is a science in which preparation starts preoperatively and continues through the postoperative phase.

Bloodless Surgery at University of Southern California University Hospital, 1997–2005

While it was at the University of Southern California (USC) University Hospital, our transfusion-free practice successfully performed >200 major surgical procedures on Jehovah’s Witnesses patients with >99% success rate, and results were detailed in several major publications in journals, including the Annals of Surgery and the Journal of the American College of Surgeons:

- Total operations performed: 850
- Number of major procedures: 350
- Mean preoperative hematocrit (major): 40%
- Mean postoperative hematocrit (major): 34%
- Mean hematocrit at discharge (major): 33%
- Mean number of days in ICU (major): 3
- Mean length (days) of hospital stay: 12

Figure 6 shows the results of the USC experience with transfusion-free liver transplantation between 1995 and 2005. Four patients were alive and well and two patients were reexplored for peritonitis. Mean length

### Table 4. Acute normovolemic hemodilution versus autologous blood donation

<table>
<thead>
<tr>
<th>Issue</th>
<th>AD</th>
<th>ANH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptable to Jehovah’s Witnesses</td>
<td>No</td>
<td>Often</td>
</tr>
<tr>
<td>ABO mismatch</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Inconvenient, expensive, or both</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Plasma/platelets wasted</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>RBC 2,3-DPG (2,3-diphosphoglycerate)</td>
<td>Low</td>
<td>Normal</td>
</tr>
<tr>
<td>Blood wastage</td>
<td>Half</td>
<td>No</td>
</tr>
</tbody>
</table>

AD = autologous donation; ANH = acute normovolemic hemodilution; RBC = red blood cell.

### Table 5. Acute normovolemic hemodilution in liver resection

<table>
<thead>
<tr>
<th></th>
<th>ANH group (n = 65)</th>
<th>Control (n =179)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>47.0 (range, 18–75)</td>
<td>55.0 (16–82)</td>
</tr>
<tr>
<td>Mean preoperative hematocrit (%)</td>
<td>37.5 (range, 28.6–50)</td>
<td>39.0 (22–48.4)</td>
</tr>
<tr>
<td>Intraoperative blood transfusion (of patients)</td>
<td>0</td>
<td>44.0 (34%)</td>
</tr>
<tr>
<td>Mean units transfused</td>
<td>0</td>
<td>3.3 (range, 1–15)</td>
</tr>
<tr>
<td>Mean postoperative hematocrit (%)</td>
<td>31.0 (range, 22.6–40.2)</td>
<td>31.3 (range, 17.9–41.2)</td>
</tr>
<tr>
<td>Mean highest postoperative bilirubin level (mg/dL)</td>
<td>3.2 (range, 0.6–36.6)</td>
<td>3.2 (range, 0.6–26.5)</td>
</tr>
<tr>
<td>Mean length of hospital stay (days)</td>
<td>7.0 (range, 4–17)</td>
<td>10.0 (range, 4–4.3)</td>
</tr>
</tbody>
</table>

ANH = acute normovolemic hemodilution.
Figure 2. Right heart (central venous pressure [CVP]) and left heart (pulmonary capillary wedge pressure [PW]) did not change (p < 0.05) with acute isovolemic anemia. Acute isovolemic reduction of hemoglobin concentration to 50 g/L decreased systemic vascular resistance index (SVRI; p < .001) by 58%.\textsuperscript{19}

Figure 3. Acute isovolemic reduction of hemoglobin concentration to 50 g/L increased heart rate (p < .001), stroke volume index (p < .001) and cardiac index (p < .001).\textsuperscript{19}

Figure 4. Acute isovolemic reduction of hemoglobin concentration to 50 g/L decreased oxygen transport rate (TO2; p < .001) and mixed venous oxyhemoglobin saturation (SvO2; p < .001).\textsuperscript{19}

Figure 5. Acute isovolemic reduction of hemoglobin concentration to 50 g/L increased oxygen consumption (VO2, p < .001) but did not change plasma lactate concentration (p = .09).\textsuperscript{19}

of hospital stay was 40.2 days (range, 8–86 days). Two patients died perioperatively; both had associated kidney failure and were receiving dialysis.

The efforts made at minimizing transfusion while maintaining hemodynamic stability since the initiation of the transfusion-free surgery program have been extremely successful (Figure 7). The use of ANH, in our experience, has decreased mean length of hospital stay and positively affected other postoperative parameters. In addition to our positive outcomes, we have successfully and dramatically decreased our use of blood and blood products. Since the implementation of transfusion-free services for liver transplantation in patients who are Jehovah’s Witnesses, we have successfully implemented similar techniques and programs for a variety of other surgical procedures and subspecialties with similar success.

Implementation of Blood-Management Programs: Administrative Schematic

We have entered a new era of patient management in which physicians and hospitals are increasingly accountable for the way that medicine is practiced (transparency; reimbursement tied to outcomes). Hospitals are no longer given a blank check to directly bill insurers for consumables. Instead of relying on direct pass-through costs to insurers, hospital reimbursement formulas are more often being structured as case rates or per diem reimbursement. This translates into fewer pass-through costs, making hospitals directly accountable for resource use. In turn, hospital administrators are now more interested in regulating physicians’ use of expensive pharmaceuticals, blood products, and devices and have encouraged them to develop oversight strategies to standardize practice, eliminate outlier use patterns, and enforce the practice of evidence-based medicine. Hospital-based committees—pharmacy and therapeutics, tissue and transfusion, surgical device, and utilization review committees—have been established for data tracking, quality control, and peer review. In this fashion, the casual administration of parenteral nutrition, intravenous antibiotics, monoclonal antibodies, and blood products, use of surgical devices, and allowance of extended lengths of stay have been curtailed.

The success of a blood-management program is predicated on the same logic: Develop a critical pathway for blood conservation (or strict transfusion avoidance), set parameters and safety methods, elaborate on data tracking, use peer review, and set up an education system, and observe the results. The committee and its component parts act to promote and enforce its initiatives with the hospital.

We have established an effective algorithm for the development and execution of a blood-management program that includes both blood-conservation and transfusion-free services. In this way, the algorithm can be used by a hospital for, at the very least, low-complexity blood-conservation services for the mainstream public. On the other hand, the very same algorithm can also be used for those hospitals that choose to pursue the more complex transfusion-free services to cater to the population of Jehovah’s Witnesses.

The overall process can be broken down into three separate phases: the initial phase, which is the purview of the process committee; the second phase, overseen by the implementation committee; and the third, or maintenance, phase.
Step 1. Initial Organization
The first step is the formation of a process committee composed of representatives from various hospital services that meet and formulate policies and procedures for:

- **Administrative identification** of patient participants depending on their portal of entry (nursing, admitting, outpatient services, blood bank, medical records, OR personnel, Jehovah’s Witnesses services director).
- **Language and legality** of consent forms that include both refusal and acceptance of blood products (legal, medical records, administration, risk management, Jehovah’s Witnesses).
- **Tracking of product administration**, including both allogeneic and ANH blood and blood products (physician leaders, data tracking, blood bank, quality assurance or performance improvement).
- **Education and awareness programs** for nurses, physicians, and ancillary personnel to foster better understanding of the blood-conservation strategies as well as of the religious beliefs and preferences of their patients (physician leaders, continuing medical education, nursing, marketing).

Step 2. Implementation
Step 2 occurs once the process committee has formalized the policies and procedures that govern patient traffic, blood-product allocation, and legal issues. Of course, the actions of the process committee are crucial if a transfusion-free program is implemented, and the need for proper patient tracking and identification, as well as the appropriate legal documents and procedures, cannot be stressed enough. However, these more intricate tasks are less important in the setting of establishing a more simple blood-management program. The implementation committee is responsible for:

- **Educational certification programs**, including a formal physician testing process that covers clinical and administrative information related to the program. This certification will allow physicians’ entry into the program (physician leaders, continuing medical education group).
- **Awareness programs** that provide promotional and broad public education to Jehovah’s Witnesses or the general public. This includes a yearly symposium about the nature of the program and other services offered (marketing, business development, physician leaders, Jehovah’s Witnesses liaison services).
- **Performance-improvement projects** to identify and track decreases in blood product use, increases in ANH and preoperative blood-augmentation practices, and corresponding changes in costs (quality assurance or performance improvement, data tracking, pharmacy services).
- **Marketing and business development** composed of Web site development, managed care relations, marketing, and liaison services for the Jehovah’s Witnesses community (marketing, business development).
- **Peer review and standards** that establish an evidence-based standard for general blood-product administration and the review of unusual cases (blood bank and laboratory, physician leaders, quality assurance or performance improvement).

Step 3. Maintenance
The maintenance phase is a continuation of the committees, procedures, and standards of care created by the implementation team. It is carried out by the various committees and should be supervised by a core group of physicians and professionals particularly interested in promoting the standards of transfusion-avoidance practice (Figure 8).

**Practical Development of a Hospital Level Blood-Management Program**
Implementation of a blood-management program should be done in steps, allowing both medical and hospital staff to adapt to the new policies and procedures in a methodical manner. This is accomplished through work...
done by the initial team meeting, setting implementation guidelines, and addressing other issues.

**Initial Team Meeting**

The initial team meeting is crucial to the successful establishment of the blood-management program. The goal of the meeting is to establish an action plan and an adequate, realistic timeframe for policy implementation. With this goal in mind, the following tasks should be completed in this meeting:

- Outline the action plan with a specific timeframe to ensure adequate completion; present the action plan and timeframe to the action-team, department directors, and relevant medical staff
- Present findings from surgery and critical care to the initiative team
- Initiate clinical and medical staff education programs; consider inviting a physician speaker to conduct medical staff education
- Obtain and establish proper approval for new blood-conservation strategies; consider scheduling ad hoc medical staff committee meeting(s) to expedite approval process
- Establish and implement new policies, including transfusion triggers
- Review the results-tracking tools
- Assess baseline spending and management of potential savings targets; keep goal in mind to share savings target and quality matrices with physicians and hospital staff monthly
- Outline an action plan to shift autologous blood donation to freestanding blood banks
- Identify necessary physician involvement to ensure proper patient notification
- Develop and share implementation guidelines (see section on this topic)
- Celebrate success as milestones are met.

After the initial team meeting and successful creation and implementation of a plan and realistic timeline, the following steps should be considered crucial key principles:

- Establishment of a hospital-based committee that deals with transfusion and blood banking to monitor costs and quality indicators that include:
  - Cross-match-to-transfusion (C.T) ratios by specialty
  - Transfusion reactions
  - Annual blood usage by category and cost per unit
  - Cell salvage and subsequent autotransfusion
  - Top five surgical procedures that routinely use blood products
  - Current use and costs associated with ICS
  - Baseline use of cell salvage by surgical procedure
- High-volume physicians in Orthopedic, Spine, Cardiovascular, and Oncology Departments that routinely type and cross for blood product
- Top five diagnoses requiring blood transfusion, including number of units routinely typed and crossed per procedure vs infused.
- Provision of the hospital staff with educational sessions on blood conservation and management programs
- Ensuring that the chief executive office (CEO), chief nursing officer, and physician initiative champions are involved and supportive of efforts. This critical step is essential to the success of the program
- Implementation of perioperative blood-conservation guidelines and considerations such as ICS, autologous transfusion, and ANH
- Adoption of a general hospital policy on universal avoidance of blood transfusion* [Jehovah’s Witnesses]
- Sharing of working definitions and “frequently asked questions” sheets with key stakeholders.

*The following recommendations should be implemented to realize prompt benefit to patient and hospital:
- Decreasing transfusion trigger to 7.0 g/dL
- Monitoring usage to establish baseline
- Ensuring that departmental leaders assess staff participation and identify those with concerns about blood conservation. Address these issues on an individual basis
- Selecting a multidisciplinary committee of medical staff leadership that includes staff and physicians from anesthesia, nursing, the laboratory, the blood bank, surgery, oncology, and pharmacy
- Preparing for an initial meeting. Collect for review all policies related to blood and blood-product administration. Data collected should include cell-saver setup, supply cost per procedure, amount of blood collected, and amount of blood transfused, labor cost associated with cell saver (hospital staff or outside contractor such as perfusion or anesthsia)
- Establishing a tracking tool. Determine the frequency of blood draws in critical care environment
- Considering the use of low-volume draw primary tubes and appropriate instrumentation in the laboratory for accuracy, reproducibility, fast turnaround times, and microvolume analysis to reduce incidence of ICU anemia
- Determining use of autologous blood (number of units received vs transfused). Identify steps to move autologous blood donation to local blood banks to reduce hospital’s indirect expense for donation and preparation
- Establishing a blood-management team weekly meeting schedule. The goals should be to adopt blood-manage-
ment standards to facility policy and to expedite policy approvals through appropriate hospital and medical staff committees for review and approval.

Implementation Guidelines
The development of specific implementation guidelines will help expedite the establishment of a complete and effective blood-management program. These are some implementation guidelines that we recommend:

- Ensuring adequate comprehension of hospital’s current blood and blood product transfusion policies, practices, and actual utilization
- Monitoring monthly blood spending, expired blood products, and existing cross match to C:T ratios
- Implementing regular communication with hospital/medical staff concerning progress of program; CEO to write letter(s) to hospital and medical staff supporting blood-management conservation program
- Reviewing blood requirements for all laboratory testing
- Developing minimum and average blood volume for each laboratory test
- Reviewing blood collection tubes and catalogue for proper tube and volume draw measurements; make recommendations to lab and medical directors
- Setting up purchasing protocols for new tubes
- Creating education plans using charts and posters; consider enlisting vendor representatives to provide visual aids
- Scheduling educational events to introduce new procedures and tubes for low-volume blood collection
- Creating plan to continuously monitor educational objectives and evaluate success of program; report to quality management committees on outcome.

Other Issues
Cell Salvage: Cell salvage is a blood-collection process that allows the surgical team to collect blood lost during a procedure, filter it, and return it to the patient intraoperatively. Fresh, autologous blood is recommended as a patient’s first option for blood transfusion in surgery; however cell salvage is a technique that can be of particular benefit in a blood-conservation program. If an institution does not already have a cell-salvage protocol in place, we make the following recommendations to help establish an effective cell-salvage program:

- Reviewing blood bank and OR records to identify procedures regularly requiring blood transfusion to create a list of procedures that might require cell-salvage equipment
- Properly training appropriate staff to manage and monitor equipment. Monitoring may be done by a perfusionist, nurse, or OR tech. The filtering and return of blood is traditionally the responsibility of the circulating nurse, anesthesiologist, or perfusionist
- Reviewing the current management and use of cell-salvage technology; cell-salvage equipment vendors may help assist with staff education as well as provide current information on benefits to blood-conservation strategies
- Using cell-saver log to begin data collection.

Anesthesia Management: Clear communication with the anesthesiologist is vital to the management and maintenance of a patient’s hematologic system. The role of the anesthesiologist in blood management is critical, given his or her involvement in intraoperative cell salvage and ANH. During transfusion-free surgery, anesthesia should maintain the normovolemic status and handle the potential need for hypervolemic and controlled hypotensive anesthesia. For example, a low central venous pressure may markedly reduce blood loss during parenchymal transection for liver resection. Similarly, blood loss during spinal surgery can be significantly curtailed by relative hypotensive anesthesia. The avoidance of hypothermia can help avoid temperature-related coagulopathy.

Conclusion
As physicians and health care professionals bound by an ethical and professional responsibility to treat patients of all faiths and beliefs, we found ourselves developing a new science, a practice that was able to maintain safety in a transfusion-free setting while performing some of the most complex and intricate surgical procedures. Through our experience, we were able to develop a process that efficiently and effectively establishes a transfusion-free program. What we realized, however, is that there are benefits to practicing in a setting that lies on a spectrum closer to being transfusion-free, where specific and calculated efforts are made to reduce the amount of allogeneic blood that is transfused, even for those who have no moral obligation for avoidance. Through effective blood management that minimizes the use of allogeneic blood and blood products, there is increased patient safety, better resource allocation, and minimization of financial burden. A strategy similar to establishing a transfusion-free program can be simplified, as outlined in this paper, and implemented to create a blood-management program that works in a similar manner, without some of the legal and moral complexities involved in maintaining
Blood-Management Programs: A Clinical and Administrative Model with Program Implementation Strategies

a transfusion-free program. Blood management is an enlightened approach to medical and surgical treatment and is based on proven and effective methods. It can be used not only to benefit the Jehovah’s Witness population but also to benefit the general population, through better use of resources.

Disclosure Statement
The author(s) have no conflicts of interest to disclose.

Acknowledgment
Katharine O’Moore-Klopf, ELS, of KOK Edit provided editorial assistance.

References
“Child is the Father of the Man”
6x18” Mixed Media Collage

By Marsha Balian, NP

This piece uses various papers, permanent marker, and acrylic paint. It resides with its owner in Umbria, Italy.

Ms Balian is a Nurse Practitioner in the Ob/Gyn Department at the Oakland Medical Center in California. Her artwork can also be seen on the cover and page 77 and on her Web site: www.marshabalian.com.
Medical, Surgical, and Endoscopic Management of Gastroesophageal Reflux Disease

Deron J Tessier, MD

Introduction

Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal diseases facing society today. In the US alone, more than 19 million people have the disease. Approximately 20% of US adults have one episode of GERD in a week, with about 7% reporting significant daily heartburn symptoms requiring some type of treatment. Medical treatments for GERD, both prescription and over the counter, cost approximately $19 billion per year in the US. Fortunately the majority of GERD symptoms are minor and self-limiting; however, complications, including esophagitis, Barrett syndrome, and adenocarcinoma, are on the rise in Western countries, suggesting that GERD does not have a benign course in all patients. The term nonerosive reflux disease (NERD) has been used to describe the majority of patients that have a benign, uncomplicated disease course. This group has GERD symptoms without evidence of esophagitis on endoscopy.

The clinical management of GERD has evolved rapidly since the early 1990s with the introduction of potent medications as well as less invasive surgical techniques to help treat patients with medically refractory disease. Novel medications to help prevent transient lower esophageal sphincter relaxations (tLESRs) are being developed and may be added to the armamentarium. Additionally, endoscopic therapies have gained some support, though long-term data suggest that these techniques are not durable.

This article reviews the pathophysiology, presentation, workup, treatment, and emerging therapies for GERD with an emphasis on surgical management and outcomes to help primary care physicians have a better understanding of the role of surgery in this complex disease.

Terminology

The classification of GERD has been confusing because of numerous definitions based on symptomatic, physiologic, and/or diagnostic criteria. In simplistic terms, GERD refers to the pathologic reflux of gastric contents into the esophagus through the gastroesophageal junction. This refluxate can be acidic, neutral, or basic (bile). It can be gas, liquid, semisolid, or a combination. The operative term in this definition is pathologic, in that belching and vomiting would not be considered pathologic because they are typically isolated events. Previously GERD was defined as a reflux event resulting in a decrease in pH of <4, several centimeters above the gastroesophageal junction. With introduction of impedance testing (see below), this definition will likely be abandoned as our knowledge of nonacid reflux comes into focus.

Pathophysiology

The normal anatomy of the gastroesophageal junction allows for relaxation of the lower esophageal sphincter (LES) as a bolus of food approaches the distal esophagus. Once the bolus is passed into the stomach, the LES contracts and remains a zone of high pressure until another bolus is swallowed. In patients with GERD, the tLESR is not coordinated with a swallow and can occur spontaneously, allowing for gastric contents to reflux into the distal esophagus. Additionally, the tLESR lasts several seconds in healthy patients, but in those with GERD, it can last more than ten seconds, resulting in significant gastric reflux. Studies have also shown that patients with pathologic GERD have more frequent tLESRs than healthy people do. Why this occurs in some people and not others is currently under investigation.

In healthy people, the LES has a baseline pressure preventing the reflux of gastric contents into the esophagus. In patients with GERD, the baseline LES pressure is lower, which increases the likelihood of reflux events. This is worse in patients who tend to eat a large meal,
which increases the intragastric pressure more than that of the LES, resulting in GERD. Esophageal body dysmotility does not directly result in GERD; however, if a patient has poor esophageal emptying, this can result in delayed clearance of esophageal contents when a reflux event occurs. The longer a refluxate is allowed to come in contact with the esophageal mucosa, the more damage it can produce. Similarly, delayed gastric emptying is known to increase the transit time of gastric contents into the duodenum. Stasis of gastric contents in the stomach of patients with gastroparesis who also have tLESR, LES hypotension, or both may result in more frequent and prolonged GERD events. Finally, a hiatal hernia is strongly associated with GERD most likely caused by a breakdown in the LES mechanism, resulting in decreased LES pressure.

Risk factors for GERD are numerous, and each likely plays some role in increasing the frequency and length of tLESR (Table 1). Obesity, for instance, is known to be a risk factor for increased reflux, and tLESR is likely due to larger meals, which result in gastric distention, increased acid production, increased intra-abdominal pressure from larger girth, or increased relaxation due to higher levels of certain hormones (eg, estrogen) that stimulate tLESR. Foods and beverages known to either relax the LES or irritate the distal esophagus include citrus drinks, spicy food, caffeinated beverages (tea, cola, coffee), chocolate, and peppermint. Patients who eat large fatty meals will also have worse symptoms most likely because of increased acid production with associated decreased LES pressure. Mediations known to exacerbate GERD by decreasing the LES pressure include calcium-channel blockers, theophylline, meperidine, some oral contraceptives, and nitrates.

**Presentation**

The presentation of GERD is fairly characteristic, with the majority of patients treating their condition before they come to clinical attention. The most common presentation is a burning pain arising from the epigastrium and radiating retrosternally to the throat and neck. Meals (especially those containing some of the already-described foods), recumbency, and bending over worsen the symptoms, whereas antacids, milk, and sitting or standing up relieve the symptoms. Patients report acidic fluid coming up to the mouth and at times the sensation that solid material is coming back up. Frank vomiting is rare in uncomplicated GERD and should raise suspicion for another underlying disease. It is not uncommon for patients to present with chest pain; however, all patients deserve an appropriate cardiac workup before their chest pain is attributed to GERD.

**Evaluation**

The mainstay in diagnosing GERD involves six-week trial of empiric therapy with a proton pump inhibitor (PPI). Patients should be reassessed after the trial to determine improvement. If symptoms have decreased, then no further workup is required and patients may continue taking the PPI either continuously or intermittently as needed. If, however, the patient’s disease responds inadequately, then further testing is necessary. The next step is to perform esophagogastroduodenoscopy (EGD). This strategy has been found to adequately diagnose GERD with a sensitivity of 75% and a specificity of 80%.

**Table 1. Potential causes of gastroesophageal reflux disease**

<table>
<thead>
<tr>
<th><strong>Physiologic</strong></th>
<th><strong>Anatomic</strong></th>
<th><strong>Social habits</strong></th>
<th><strong>Medications</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>LES hypotension</td>
<td>Obesity</td>
<td>Alcohol</td>
<td>Theophylline</td>
</tr>
<tr>
<td>Transient LES relaxation</td>
<td>Hiatal hernia</td>
<td>Smoking</td>
<td>Nitrates</td>
</tr>
<tr>
<td>Esophageal dysmotility</td>
<td></td>
<td>Stress</td>
<td>Meperidine</td>
</tr>
<tr>
<td>Delayed gastric emptying</td>
<td></td>
<td>High-fat diet</td>
<td>Calcium-channel blockers</td>
</tr>
<tr>
<td>Hyperchlorhydria</td>
<td></td>
<td>Chocolate</td>
<td>Meperidine</td>
</tr>
<tr>
<td><em>Helicobacter pylori</em></td>
<td></td>
<td>Caffeine and coffee</td>
<td>Nonsteroidal anti-inflammatory drugs</td>
</tr>
<tr>
<td>Duodenogastroesophageal reflux</td>
<td></td>
<td></td>
<td>Oral contraceptives</td>
</tr>
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</table>

LES = lower esophageal sphincter.
ease other than GERD. Some notable exceptions to this strategy include patients with alarm symptoms who are likely to have a more serious lesion, patients older than age 55 years who may have a higher risk of a serious lesion, and patients taking esophagotoxic medications such as nonsteroidal anti-inflammatory drugs and bisphosphonates who may have a complication related to their medication. If patients’ disease responds minimally or not at all to PPIs and they undergo EGD and no abnormality is found to explain their symptoms, then the workup should be directed at the differential for dyspepsia (Table 2).

As already mentioned, EGD is the standard clinical test for GERD and an important test in patients with alarm symptoms. It is highly sensitive and specific for esophagitis and complications of GERD such as ulcerative disease. EGD allows the ability to determine the exact extent of mucosal injury and is capable of performing biopsy if necessary. EGD allows identification of Barrett esophagus because of the characteristic salmon color of the mucosa on endoscopy, and biopsy allows pathologic staging.

Ambulatory pH monitoring is the most sensitive test for acid reflux, but it does not detect nonacid reflux events. The standard test requires placement of a nasal pH probe that monitors esophageal pH for 24 hours while the patient resumes his or her usual diet and activities. The patient then documents activities and esophageal symptoms either in a diary or with an external monitoring system. At the completion of the study, the patient’s symptoms are correlated with the pH monitoring results and several criteria are used to determine the extent of the patient’s reflux disease. This test should be used only to confirm acid reflux if surgery is anticipated or to optimize medical treatment in patients with continued symptoms while taking PPIs. If surgery is anticipated, then the study should be performed while the patient has discontinued PPI therapy to allow documentation of the exact severity of acid reflux. If patients continue taking their PPI, then the study may produce false negative results. If surgery is not anticipated but the clinician would like to determine whether the patient’s medical treatment is optimum, then the study should be performed while the patient is still taking a PPI to determine whether the patient is having asymptomatic acid reflux. Newer technology allows for a small pH probe to be placed 6 cm above the gastroesophageal junction, which then sends signals to an external monitoring system. This allows both for more comfort for the patient and for longer monitoring times (48 hours).

A barium esophagram can be ordered to evaluate a patient with suspected GERD; it may demonstrate a GERD episode, detect esophageal mucosal injury, and identify a sliding or paraesophageal hernia. It may also exclude complications of GERD, such as esophagitis, stricture, ulcers, and adenocarcinoma. EGD has largely replaced the barium esophagram as a diagnostic test in GERD because of its higher sensitivity and ability to obtain tissue for diagnosis. The best use of a barium esophagram is in patients presenting with dysphagia, because the test has a better sensitivity than other tests for diagnosing Schatzki rings, webs, diverticula, and strictures.

Although acid reflux is what most clinicians think causes GERD, recent evidence has shown that nonacid reflux may be just as detrimental to the esophageal mucosa. Bile in duodenogastroesophageal reflux has been associated with Barrett esophagus. Monitoring of bile levels by using a miniature fiberoptic probe (such as the Bilitech device from Medtronic, Minneapolis, MN, US) can be performed on an outpatient basis. This test is not widely available, however, and should be interpreted by someone experienced in its use.

Impedance monitoring is another emerging technology that is currently being evaluated to determine nonacid reflux events. A special probe is placed nasally and used to detect changes in the electrical conductance of the intraluminal contents of the esophagus. This allows the physician to determine what substance (liquid, solid, gas) is passing through the esophagus as well as which direction it is going (antegrade or retrograde). For instance, swallowed liquid will cause an antegrade decrease in impedance, whereas liquid reflux produces a retrograde decrease in impedance regardless of pH. Several small studies have shown, through impedance monitoring, that in GERD that does not respond to PPIs, the underlying process is nonacid GERD. Again, this technology is not widely available and requires experienced clinicians to meaningfully interpret the results before making recommendations for treatment.

Table 2. Differential diagnosis for dyspepsia

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Cholelithiasis</td>
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<tr>
<td>Cholelitholitiasis</td>
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<tr>
<td>Acute viral hepatitis</td>
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<tr>
<td>Alcoholic hepatitis</td>
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<tr>
<td>Acute pancreatitis</td>
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<tr>
<td>Gastroduodenal ulcers</td>
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<td>Gastritis</td>
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<tr>
<td>Pyelonephritis</td>
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<tr>
<td>Nephrolithiasis</td>
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<tr>
<td>Shingles</td>
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<tr>
<td>Mesenteric ischemia</td>
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Medical, Surgical, and Endoscopic Management of Gastroesophageal Reflux Disease
Esophageal manometry is an important test to perform especially in those patients with abnormal esophageal complaints or those patients desiring surgical intervention for GERD. In patients with atypical GERD symptoms that are refractory to PPIs, manometry may help diagnose achalasia, esophageal spasm, or other esophageal motility disorders. In patients desiring surgery, manometry should be performed to document normal peristalsis before fundoplication.

Treatment Overview
The goals for treatment of GERD are to resolve symptoms, heal esophagitis and ulcers, and prevent complications such as stricture, Barrett esophagus, and bleeding. Strictures are known to occur in 0.1% of patients and occur most often in males, whites, and older patients. Barrett esophagus occurs as a complication of GERD and is characterized by the replacement of the distal squamous esophageal mucosa with intestinal metaplasia. Barrett esophagus is uncommonly found in patients younger than age 50 but is found in up to 2% of patients older than age 50 who are referred for endoscopy. The etiology of Barrett esophagus is unknown, but the most popular theory suggests that it is the mucosa’s attempt to adapt to the long-term reflux of gastric contents. Although esophagitis without the changes of Barrett disease is not associated with esophageal adenocarcinoma, patients with changes from Barrett disease have a 1% per year risk of developing adenocarcinoma.

Medical and surgical therapies have varying success rates. Reports of study results favoring each modality have been widely published and touted by their proponents. It is more likely that medical, surgical, and potentially endoscopic therapies all play a role in the management of GERD; the following discussion will help primary care physicians and gastroenterologists decide which modality is best for a particular patient.

Lifestyle and Dietary Modifications
Minor GERD symptoms can be initially treated with simple lifestyle and dietary modifications. Elevating the head of the bed (at least six inches) can help prevent nighttime symptoms. Additionally, avoiding late-night snacks and eating small dinners can help treat minor nighttime symptoms. Avoiding clothes that fit tightly around the mid-abdomen may help occasional symptoms as well. Avoidance of foods that increase reflux events or are caustic to the esophageal mucosa, as mentioned earlier, can help reduce symptoms. Weight loss can produce dramatic results in some patients; however, patients overweight for a long time have a high rate of weight regain and subsequent recurrence of GERD symptoms. Smoking and alcohol use should be reduced or ideally completely stopped. Although stress has not been shown to increase the frequency of GERD events, patients’ perception of GERD is increased during high stress events. Patients should be encouraged to avoid stressful situations at either work or home. Because GERD seems to be a progressive disease, it is likely that many patients will require medical therapy at some point.

Medical Therapy

Antacids and Proton Pump Inhibitors
Traditionally, many patients have self-medicated with over-the-counter antacids before they seek medical attention. Antacids are generally quick and effective for intermittent symptoms. H₂-blockers were the first medical treatment for GERD that showed substantial improvement over antacids for the chronic GERD. H₂-blockers have also made their way into self-medication, with the general public being able to buy them over the counter. The limitations of H₂-blockers include twice-daily dosing and limited response in moderate esophagitis (75%). PPIs have become the preferred medical therapy for erosive esophagitis because they produce a higher rate of response (80%–95%).

PPIs, which act by blocking the hydrogen potassium adenosine triphosphatase, are typically given only once a day. Side effects are minimal and include diarrhea and headaches. PPIs have been shown to be both safe and effective, even when taken for long periods. Chronic PPI therapy has been associated with small reductions in vitamin B₁₂ levels because of decreases in protein-bound vitamin B₁₂ absorption. There has been an association of chronic PPI use with an increase in community-acquired pneumonias and Clostridium difficile infection. PPIs are not meant for patients with intermittent GERD, as the medications can take several hours to take effect.

Once patients have had symptom remission for more than two or three months, a trial of tapering their dosage can be attempted. Patients taking PPIs twice daily should taper to once daily, whereas patients taking PPIs once daily can switch to twice-daily H₂-blockers. Patients taking H₂-blockers can have their dose tapered in a similar manner, with a gradual reduction in dosage to prevent symptoms from flaring up. This process can take anywhere from two to six months, depending on the individual patient’s response and tolerance to the medication.
manner. If a patient is found to have erosive esophagitis, then that patient should be monitored with endoscopy during the tapering phase to determine if remission is occurring at the mucosal level as well as the symptomatic level. The majority of patients taking PPIs for esophagitis will require long-term—if not lifetime—therapy with the lowest dose of either PPIs or H₂-blockers. Acute cessation of PPI therapy should be avoided, as there is a rebound hypersecretion of acid when the medication is abruptly stopped.

Limitations of Medical Therapy

Although PPIs have been found to be both safe and effective for GERD, current studies suggest that in approximately 30% of patients, the disease responds incompletely or, in some cases, not at all to therapy. Mechanisms of failure include poor compliance, visceral hypersensitivity, duodenogastroesophageal reflux, nonacid reflux disease, delayed gastric emptying, PPI resistance, and poor bioavailability. Additionally, in patients with psychologic disorders and concomitant bowel disorders, PPI therapy may fail. These patients will likely benefit more from treatment of their underlying psychologic and bowel disorders. In patients with erosive esophagitis, there is a small group of patients whose esophagitis heals but who continue to have significant symptoms (27%). Additionally, 80% of patients with erosive esophagitis have a relapse of their symptoms within 6 to 12 months after cessation of medical therapy. In a large review of published study results, the overall relapse rate of erosive esophagitis in patients treated with PPIs was 22% and in those treated with H₂-blockers was 58%.

Surgical Therapy Techniques

GERD has been treated surgically since the early 1950s, with the most common procedure being the Nissen fundoplication. Other procedures include the Hill, Belsey, and Toupet repairs. A complete review of all of these techniques and their outcomes is beyond the scope of this review. Unless otherwise stated, the data presented here are from studies of the Nissen fundoplication.

In the era of open antireflux operations, symptom response rates of 80% to 90% were commonly reported. Many patients, however, did not undergo surgical intervention because of the high morbidity of the procedure. With the introduction of laparoscopic techniques, there was an exponential growth in the number of antireflux operations despite no clear evidence of its superiority. Recent long-term studies have confirmed that laparoscopic fundoplication is not only as effective as open surgery but also results in fewer incisional hernias, shorter hospital stays, less pain, quicker return to work, and fewer defective wraps at follow-up endoscopy. Laparoscopic fundoplication has fallen out of favor as a primary treatment for GERD since the introduction of more potent medical therapy.

Although medical therapy is the first-line therapy for GERD, there are still select indications for surgical treatment (Table 3). Because GERD is a chronic condition that is due to a mechanical failure of the antireflux mechanism and because current medical treatment is directed only at the suppression of acid, there is concern about the effectiveness of long-term medical therapy. As mentioned earlier, current data show that not all GERD is due to acid reflux. Alkaline reflux likely contributes to esophagitis and possibly Barrett esophagus. Because GERD is a chronic condition, most patients will require intermittent if not lifetime therapy. The expense, the psychologic burden of a lifetime of medical therapy, and the uncertainty of the long-term effects of a lifetime of medical therapy should be addressed with all patients considering long-term medication use. Patients who are averse to surgery and get excellent results with

<table>
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<tr>
<th>Table 3. Indications for surgical referral for GERD</th>
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<tr>
<td><strong>Failure of medical therapy</strong></td>
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<tr>
<td>Complications of GERD</td>
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<tr>
<td>Stricture</td>
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<tr>
<td>Barrett esophagus</td>
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<tr>
<td>Bleeding</td>
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<tr>
<td>Recurrent esophagitis despite medical therapy</td>
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<tr>
<td><strong>Patient not wanting lifelong medication</strong></td>
</tr>
<tr>
<td>Atypical symptoms</td>
</tr>
<tr>
<td>Asthma related to GERD</td>
</tr>
<tr>
<td>Hoarseness</td>
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<tr>
<td>Chronic cough</td>
</tr>
<tr>
<td>Noncardiac chest pain</td>
</tr>
<tr>
<td>Recurrent aspiration pneumonia</td>
</tr>
<tr>
<td><strong>Medical problems attributable to a large hiatal hernia</strong></td>
</tr>
<tr>
<td>Bleeding</td>
</tr>
<tr>
<td>Dysphagia</td>
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</tbody>
</table>

GERD = gastroesophageal reflux disease.
medications can be monitored safely. If patients have any uncertainty about taking medications and would like to explore surgical options, they should be referred to an experienced esophageal surgeon. This is especially true for young patients who face taking medications for 30 to 50 years, especially if they get excellent results with medications. These are the ideal candidates for antireflux surgery, with success rates approaching 90% in experienced hands. The opposite is true for patients who have limited life expectancy; these patients are best suited for medical treatment.

Other patients who should be evaluated for surgical therapy include those in whom medical management has failed, those with complications of GERD (e.g., esophagitis not responding to medical therapy, Barrett esophagus, stricture), and those with medical complications attributable to a large hiatal hernia, such as bleeding and dysphagia. Those patients with atypical symptoms of GERD such as asthma, hoarseness, cough, noncardiac chest pain, and recurrent aspiration pneumonia may also benefit from surgery. It is very important that a complete workup, including a 24-hour pH study, be performed in these patients to confirm acid reflux.

Patients who are evaluated by their primary care providers and desire surgical intervention should be referred to an experienced esophageal surgeon. The appropriate workup in these cases begins with EGD to evaluate for esophageal complications and rule out gastric or duodenal causes for the symptoms. If EGD produces normal findings, then a 24-hour pH study while the patient is not taking medications should be performed to document acid reflux. If EGD shows esophagitis, a pH study is not mandatory. Before surgery, a motility study is paramount to evaluate the contractility of the patient’s esophagus. If this shows weak peristalsis, then a partial wrap may be the best option for the patient. Some surgeons will also obtain upper gastrointestinal swallow studies. This is helpful only if the patient has an associated hiatal hernia to determine the size of the hernia and length of the esophagus. If findings for all of the above studies are normal but the patient still has significant symptoms, then consideration should be made to referring these patients to an institution with impedance testing or testing with a Bilitech probe to evaluate for nonacid reflux disease.

**Surgical Outcomes**

Results of laparoscopic Nissen fundoplication have been excellent in experienced hands. Conversion rates to open surgery are <5% and typically occur early in a surgeon’s experience. Patients undergoing this procedure typically spend one night in the hospital, although some studies have reported excellent results with same-day procedures. Common complaints immediately after fundoplication include early satiety (84%), bloating and flatulence (61%), and dysphagia (32%). At examination three months after surgery, however, no patients complain of early satiety, 3% have bloating, and <1% have dysphagia. Patients with continued dysphagia after three months should undergo a contrast study to determine whether the wrap has slipped, which is the usual cause for this problem (80%).

Long-term studies have shown that when patients are properly selected for surgery and undergo fundoplication by experienced surgeons, the results are excellent. Patients can expect a remission rate >90%, with no need for medical therapy. Patients who do require some medication will usually require doses that are lower and less frequent than their preoperative dose. Long-term quality-of-life studies have shown that up to 95% of patients rate their surgery outcomes as either good or excellent and would undergo the surgery again. The results for those who undergo open surgery are equivalent. The laparoscopic technique does result in lower perioperative morbidity, making it the current gold standard.

**Endoscopic Therapy**

Several endoscopic therapies have recently been developed as an alternative to surgical treatment of medically refractory GERD. The most widely studied include the Stretta device (Curon Medical, Inc, Fremont, CA), the EndoCinch suturing system (CR Bard, Inc, Murray Hill, NJ), the Enteryx system, and the Plicator (NDO Surgical, Inc, Mansfield, MA). Each of these procedures works by improving the mechanical barrier of the LES. The results from these endoscopic therapies have been generally disappointing and have limited widespread application. Although it is thought that these are relatively benign procedures, this is not the case. Indeed, the Enteryx system was voluntarily withdrawn from the market because of several deaths directly related to the procedure. The other techniques are typically done on an outpatient basis, but chest pain, dysphagia, and vomiting are some of the most common, albeit rare, complaints. Endoscopic therapies have not gained widespread application.
application, and many experts from both surgical and gastroenterology fields believe that they are still experimental.

**Conclusion**

GERD is a progressive, lifelong disease that can severely limit up to 20% of patients who have it, despite optimal medical therapy. Primary care clinicians should not assume that patients are satisfied with their medical therapy for GERD and should refer appropriate candidates to discuss surgical therapy. Laparoscopic Nissen fundoplication has proven safe and effective in long-term studies when performed by experienced esophageal surgeons. Endoscopic therapies hold out the promise of decreased morbidity and increased efficacy that has yet to be realized and thus should be limited to specialized centers under supervised protocols.

**Disclosure Statement**

The author(s) have no conflicts of interest to disclose.

**Acknowledgment**

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**References**

National Practice Recommendations for Hematuria: How to Evaluate in the Absence of Strong Evidence?

Ronald Loo, MD
Joel Whittaker, MPH
Violeta Rabrenivich, MHA, CHIE

Abstract
Hematuria is one of the most common conditions confronting clinical urologists and is present in many genitourinary pathology conditions. Although researchers have studied hematuria symptoms in an effort to determine the best diagnostic pathway, the existing lack of scientific evidence has created variations in clinical practice. The literature does not provide enough evidence to significantly alter the need to assess these patients. Consequently, many patients with microscopic or gross hematuria undergo low-yield workups that include invasive testing and imaging with radiation. In 2007, a national group of Kaiser Permanente (KP) urology chiefs agreed that national practice recommendations were needed to address existing variations in the management and workup of hematuria. Using a KP guideline methodology, the group reached a consensus agreement on the following recommendations: 1) referral to urology is recommended for all people with gross hematuria or high-grade hematuria (>50 red blood cells per high-power field [RBCs/HPF]) on a single urinalysis (UA); 2) referral to urology and urologic evaluation is recommended for men or women with asymptomatic microscopic hematuria or symptomatic hematuria that produces >3 RBCs/HPF on two of three properly performed and collected urinalyses; and 3) voided urinary cytology should be eliminated from asymptomatic microscopic hematuria or symptomatic hematuria that produces >3 RBCs/HPF on two of three properly performed and collected urinalyses; and 3) voided urinary cytology should be eliminated from asymptomatic hematuria screening protocol. The test is not sensitive enough to obviate further workup if findings are negative, and elimination of this screening test is estimated to save millions of dollars across the US. Hematuria on a UA should be reported as 0 to 3 RBC/HPF, 4 to 10 RBC/HPF, 11 to 25 RBC/HPF, 26 to 50 RBC/HPF, >50 RBC/HPF, or gross hematuria. This approach will also reduce radiation exposure.

Introduction

Background
Quality improvement requires physicians to systematically explore new scientific evidence, integrate this information into practice, and evaluate their performance. In addition, Kaiser Permanente (KP) clinicians need to effectively leverage our integrated delivery system in providing preventive care, improving early detection, and managing complex clinical conditions. Daily, clinicians face situations that require a comprehensive understanding of the complex variables involved in patient care, aggressive decision making, and prioritization of work and of resources.

The Interregional Chiefs of Urology Service (IRCUS) is one of many KP groups that embrace quality-improvement methods and activities. With support from the regional Clinical Practice Guidelines team, the national KP HealthConnect team, and The Permanente Federation, these clinicians have elected to work on several areas of focus as a national quality-improvement agenda. On the basis of an identified need and many years of clinical practice, the group decided to focus on a standardized hematuria evaluation.

Lack of Scientific Evidence
Adult microhematuria is an example of a clinical symptom for which the lack of scientific evidence has created variations in clinical practice. Hematuria is one of the most common conditions confronting clinical urologists and is present in a number of genitourinary pathology conditions. According to KP experts, it is estimated to account for 20% of all urologic visits and up to 13.9% of urologic hospitalizations.

Similar efforts to address hematuria symptoms have been initiated by professional associations and individual clinicians. In 2001, the American Urological Association (AUA) convened the Best Practice Policy
Panel on Asymptomatic Microscopic Hematuria to formulate policy statements and recommendations for the evaluation of asymptomatic microhematuria in adults. As a result of these efforts, the AUA recommended that an appropriate renal or urologic evaluation be performed for all patients with asymptomatic microscopic hematuria who are at risk for urologic disease or primary renal disease; however, there was no consensus on when to test for microscopic hematuria in the primary care setting, and screening was not addressed in this report.

In addition, the current literature does not provide enough evidence to significantly alter the need to assess these patients. Consequently, many patients undergo low-yield workups that include invasive testing and imaging with radiation.

### Methodology
IRCUS is a multidisciplinary group (Table 1) that works to ensure that KP provides safe, effective, and high-quality care; to reduce practice variation; and to create organizational improvement in urologic care. In 2007, they sponsored a review of the literature to address core clinical questions relating to hematuria management and workup (Table 2). Evaluation of recommendations issued by the AUA and input were obtained both from national and regional KP Guideline Development Units.

Although the AUA recommendations represented a consensus statement of urologists from across the US, our clinicians believed the KP guideline methodology (Common Methodology), developed by interregional guideline experts, to be more rigorous. (In accordance with KP’s Common Guideline Methodology, consensus-based recommendations are developed when an important clinical question needs to be answered and the evidence is insufficient to support evidence-based recommendations.) The group believed that the existing situation warranted development of national practice recommendations. In addition, they believed that KP,

### Table 1. The Kaiser Permanente Interregional Chiefs of Urology Service

<table>
<thead>
<tr>
<th>Region</th>
<th>Urologists</th>
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<tbody>
<tr>
<td>Colorado</td>
<td>Edward Swartz, MD</td>
</tr>
<tr>
<td>Georgia</td>
<td>David Starr, MD</td>
</tr>
<tr>
<td>Group Health Permanente; Seattle, WA</td>
<td>Marc A Lowe, MD</td>
</tr>
<tr>
<td>Hawaii</td>
<td>Howard Landa, MD</td>
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<td></td>
<td>Albert Mariani, MD</td>
</tr>
<tr>
<td></td>
<td>Michelle Aspera, MD</td>
</tr>
<tr>
<td>Ohio</td>
<td>Nabil Chehade, MD</td>
</tr>
<tr>
<td>Northern California</td>
<td>Gary Nicolaisen, MD</td>
</tr>
<tr>
<td>Northwest</td>
<td>Stephen Lieberman, MD</td>
</tr>
<tr>
<td>Southern California</td>
<td>Ron Loo, MD</td>
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<td></td>
<td>James Murphy, MD</td>
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<td>Marguerite Koster</td>
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<td>Thomas Vandergast, MD</td>
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<td>Joel Whittaker, MPH</td>
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<tr>
<td>The Permanente Federation</td>
<td>Jed Weissberg, MD</td>
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<td>Violeta Rabrenovich, MHA, CHIE</td>
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### Table 2. Core clinical questions and evidence search strategy

<table>
<thead>
<tr>
<th>Core clinical questions</th>
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<tbody>
<tr>
<td>1. For patients with microhematuria, what threshold of red blood cells per high power field (RBC/HPF) is associated with a sufficient probability of urologic pathology to warrant a referral to urology?</td>
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<tr>
<td>2. How should hematuria be reported on the urinalysis?</td>
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<tr>
<td>3. What is the role of urine cytology and/or bladder tumor markers in the detection of urologic pathology among patients with hematuria?</td>
</tr>
<tr>
<td>4. For patients with hematuria, what imaging tests (ie, CT urogram, modified CT urogram, intravenous pyelogram, helical CT, and/or renal ultrasonography) should be employed for the detection of urologic cancers?</td>
</tr>
<tr>
<td>5. Is routine urinalysis screening effective for reducing urologic pathology in the asymptomatic population?</td>
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</table>

To answer the group’s clinical questions, a literature search included the following databases and specialty sites:

- Kaiser Permanente Clinical Library
- Clinical Evidence via OVID
- PUBMED
- Hayes
- Blue Cross
- Blue Shield TEC, Health Tech Assessment database
- Southern California Permanente Medical Group Medical Tech Assessment Database
- Turning Research Into Practice database (Bandolier, Agency for Healthcare Research and Quality, New Zealand Guideline Group, Monash, National Institute for Clinical Excellence, Scottish Intercollegiate Guideline Network)
- American Urological Association
- American College of Radiology

CT = computed tomography
as an integrated delivery system, offers a unique opportunity to manage patient care across care settings in a more effective way. Finally, as with many other specialties, KP Urology Departments have a long and outstanding history of research and quality-improvement efforts that can be leveraged.

This initiative was sponsored by the Associate Executive Medical Directors—Quality, Southern California Permanente Medical Group Technology Assessment and Guideline Unit, and The Permanente Federation.

Results
Kaiser Permanente National Practice Resource

After reviewing the literature, the group concluded that evidence relating to the diagnostic follow-up care of hematuria was insufficient for developing “evidence-based” practice recommendations. Despite insufficient evidence, the clinicians agreed that consensus-based national practice recommendations were nonetheless warranted to reduce the variation in hematuria management.

Figure 1. Adult hematuria workup algorithm.

C + S = culture and sensitivity; e-gfr = estimated glomerular filtration rate; HPF = high-power field; rbc = red blood cells; iVP = intravenous pyelogram; KUB = kidneys, ureter, bladder; NSAIDs = nonsteroidal anti-inflammatory drugs; RUS = renal ultrasound; U/A = urinalysis.

1 Urine specimens should be collected >48 hours after exercise. The U/A should be analyzed fresh if possible, by a standardized methodology to avoid the lysus of formed elements from heat for chemical breakdown.

2 After urologic evaluation is completed, re-referral for persistent microhematuria is not needed unless there is a change in clinical situation, such as the occurrence of gross hematuria or another sign or symptom suggestive of possible urologic pathology.

3 CT Urogram is defined as a two-phase study (noncontrast followed by postcontrast delay) and KUB reconstruction. When IVP is ordered, clinicians should take into consideration patient history of chronic illness (diabetes, heart failure, and other comorbidities), as well as a patient being on certain medications (metformin, NSAIDs, and others).

4 Patients receiving contrast should have a serum e-gfr testing performed prior to the procedure.
The Standardized Hematuria Evaluation Practice Resource\(^3\) describes the evidence and steps for screening adult patients, the making of risk assessments, and summarizes suggested diagnostic follow-up treatment. The goals of this work—in the face of insufficient evidence—are to standardize and optimize a proper workup for patients with hematuria and to minimize radiation exposure from unnecessary testing among those patients unlikely to have serious disease (Figure 1).

An additional goal is to provide clinicians with adequate background and resources to increase their comfort in evaluating patients with asymptomatic microscopic hematuria. This practice resource is not intended to replace a clinician’s judgment or to establish a protocol for all patients with this clinical issue.

The clinicians agreed on and supported the following consensus-based recommendations.

**Recommendation 1**

Referral to urology is recommended for all patients with gross hematuria or high-grade hematuria (>50 RBC/HPF) on a single urinalysis (UA).

Referral to urology and urologic evaluation is recommended for men or women with asymptomatic microscopic hematuria or symptomatic hematuria (unilateral flank pain, lower irritative voiding symptoms, recurrent urinary tract infections despite appropriate use of antibiotics, etc) that produces >3 RBC/HPF on two of three properly performed and collected UAs. (Note: Urine specimens should be collected >48 hours after exercise. The UA should also be done when the urine is fresh if possible, by a standardized methodology, to avoid the lysis of formed elements from heat or chemical breakdown.)

**Evidence review and rationale:** A review of the evidence identified one evidence review by Southern California Permanente Medical Group (SCPMG),\(^4\) which identified 18 studies evaluating hematuria and the risk of urologic disease. Eleven of the 18 studies did not provide the data needed to evaluate urologic cancer rates at specific cutoff points below 8 RBC/HPF. Among the seven remaining studies where cutoff points of >2 to 5 RBC/HPF were used to define microhematuria, urologic or renal cancers were detected 1.3% to 8.3% of the time among patients who were older than 33 years.\(^5\) The review also examined laboratory case series studies to determine the upper limit of normal (95th percentile) among “healthy” patients receiving microscopic UA. These studies show a strong trend toward “normal” limits, ranging from 0 to 2 RBC/HPF in men and from 0 to 5 RBC/HPF in women. It is important to note that although the normal limits varied between men and women, the studies did not provide information regarding the actual presence or absence of urologic disease in the populations studied. Ultimately, the SCPMG review concluded that there is insufficient evidence to determine the “optimal” RBC/HPF cutoff point for detecting clinically significant asymptomatic microhematuria. A subsequent literature search was conducted in 2007 to update the 2003 SCPMG review. No additional systematic reviews, meta-analyses, or randomized, controlled trials (RCTs) were identified.

In the absence of high-quality RCTs or systematic reviews, the Interregional Urology Chiefs Group agreed, on a consensus basis, that referral to urology for further diagnostic workup is recommended for asymptomatic patients whose microscopic UA yields >3 RBC/HPF on two of three properly urinalyses, regardless of patient sex. The chiefs also agreed that urine samples should be collected after avoiding strenuous physical exercise for >48 hours to avoid glomerular or urothelial exercise hematuria; urine should also be analyzed fresh if possible, by a standardized methodology, to avoid the lysis of formed elements from heat or chemical breakdown. The chiefs recommend evaluating three urine specimens because of evidence from one study showing that 18% of patients with a life-threatening lesion had negative findings on at least one UA within six months of the diagnosis.\(^8\)

**Hematuria evaluation:** This evaluation should not be performed if the risk of the testing exceeds the risk of the medical condition that is diagnosed. Thus, if the life-threatening risk of a hematuria evaluation (instrumentation urosepsis, contrast anaphylaxis, radiation risk, contrast nephropathy) is greater than the yield of the evaluation for a defined population, then the evaluation should not be performed.

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**National recommendations**

1. Referral to urology is recommended for all patients with gross hematuria or high-grade hematuria (≥50 RBC/HPF) on a single urinalysis (UA).

2. Hematuria on a UA should be reported out as 0 to 3 RBC/HPF, 4 to 10 RBC/HPF, 11 to 25 RBC/HPF, 26 to 50 RBC/HPF, ≥50 RBC/HPF, or gross hematuria.

3. There was no consensus on the role of urine cytology and/or bladder tumor markers in the evaluation of patients with hematuria.

4. A modified computed tomography (CT) urogram or IVP with concurrent renal ultrasound is recommended for patients with significant hematuria.

5. There is insufficient evidence to recommend routine UA to screen for asymptomatic hematuria in the absence of clinical indicators.
Follow-up care: Hematuria is likely to persist in the majority of patients who are monitored. The evidence for the risk of cancer developing within two to five years in patients with hematuria who have been evaluated is scanty, but it is in the range of 0% to 3%.

A retrospective study (which did not distinguish between gross hematuria and microhematuria) of 823 patients who did not have a malignancy and whose medical charts were available found that the average follow-up monitoring was 14.7 years. Using intravenous pyelogram (IVP) as the lone imaging modality, transitional cell carcinoma (TCC) was found in 7 of 740 (0.95%) patients at an average of 14.3 years after diagnosis (range, 5.3–23.9 years). Renal cell carcinoma (RCC) developed in 5 of 740 (0.68%) patients at an average of 15.7 years after diagnosis (range, 2.5–23.2 years). Overall, 1.5% of the evaluated patients developed TCC or RCC. Gross hematuria or a smoking history was present in 77%. Although the data on which to base recommendations for hematuria follow-up care is limited, consideration may be given to reevaluating any patient with gross hematuria or persistent microhematuria and a smoking history at two to five years.9

Recommendation 2

Hematuria on a UA should be reported out as 0 to 3 RBC/HPF, 4 to 10 RBC/HPF, 11 to 25 RBC/HPF, 26 to 50 RBC/HPF, >50 RBC/HPF, or gross hematuria.

Evidence review and rationale: Literature sources that specifically compared the effect of reporting UA results according to varied cutoff points were not identified. One large prospective study9 of 1000 consecutive patients with asymptomatic hematuria found that the incidence of urologic pathology was greater for people with high-grade hematuria vs low-grade microhematuria; no difference between low (4–10 RBC/HPF) and intermediate grades of hematuria was found.

To gain a better understanding of how hematuria correlates with the presence or absence of urologic disease, IRCUS agreed to standardize the reporting of UA results according to the following cutoffs: 0 to 3 RBC/HPF, 4 to 10 RBC/HPF, 11 to 25 RBC/HPF, 26 to 50 RBC/HPF, >50 RBC/HPF, or gross hematuria. Examination of UA data that are reported in a standard fashion may provide insight to clinicians on how to best to stratify hematuria workups on the basis of the yield of urologic disease in each category.

Recommendation 3

There was no consensus on the role of urine cytology and/or bladder tumor markers in the evaluation of patients with hematuria.

Evidence review and rationale: A literature search was conducted to identify studies evaluating the effectiveness of urine cytology and bladder tumor markers for the detection of urologic cancer among patients with hematuria. Several systematic reviews were identified.

One systematic review11-15 identified 15 studies evaluating urine cytology and NMP22 BladderChek Test (Matritech, Inc, Newton, MA, USA) as tests for detecting urinary tract malignancy. Pooled data from these studies showed that sensitivity for the urine cytology test ranged from 3% to 100%, whereas specificity ranged from 62% to 100%. The review also found inconsistent data from five heterogeneous studies regarding the sensitivity (58%–91%) and specificity (60%–84%) of the NMP22 BladderChek Test for the detection of urologic disease. The authors caution against drawing definitive conclusions, given that the studies included were heterogeneous, methodologically flawed, and subject to potential bias. Ultimately, the study authors agreed with the AUA statement that the available data are insufficient to recommend routine use of voided urinary markers in patients with microscopic hematuria.

In 2005, the KP Southern California Technology Assessment and Guidelines Team reviewed the literature for the use of the NMP22 BladderChek Test to detect primary or recurrent TCC of the urinary tract.9 No RCTs were identified. They did, however, find 22 uncontrolled studies evaluating the accuracy of the test. The NMP22 BladderChek Test had a sensitivity ranging from 30% to 100%, specificity of 60% to 90%, and positive predictive value (PPV) of 34% to 76%. The team concluded that the sensitivity of the NMP22 BladderChek Test suggests that it may help to detect low-grade primary carcinomas, but the specificity and PPV of the NMP22 BladderChek Test also suggest that the test would result in an increased number of unnecessary cystoscopic procedures. However, most results highlight increased specificity and sensitivity.14

Another systematic review15 pooled data from 42 studies (n = 5706) and compared the diagnostic accuracy of urine cytology vs other tests (BTA [Polymedco, Inc, Cortlandt Manor, NY, USA], BTA stat [Polymedco, Inc], BTA TRAK [Polymedco, Inc], telomerase, or NMP22 BladderChek Test) against the reference standard of cystoscopy and/or histopathology. They found that cytology had a pooled specificity of 94%, which was

These studies show a strong trend toward “normal” limits ranging from 0 to 2 RBC/HPF in males and from 0 to 5 RBC/HPF in females.
The purpose of a bladder tumor marker is to increase the clinician's index of suspicion for TCC of the urinary tract. Questions have been raised about the appropriate-ness of urine cytology as part of a hematuria study. This was studied from the KP Hawaii Hematuria 1000-patient hematuria database. We found a sensitivity of 55% and a specificity of 99.3%. Unique information that led to a diagnosis of urinary tract TCC was found in four patients. The cost to diagnose a cancer by this test and no other (unique information) in the hematuria evaluation was $8367 vs $5616 for IVP, $3235 for cystoscopy, and $3291 for creatinine. The cost of the test to diagnose a life-threatening lesion (in support of other tests whose findings might also have made the diagnosis) was $1521 for cytology, $1695 for IVP, $3044 for cystoscopy, and $3291 for creatinine. This study supported the use of urine cytology in that it diagnosed TCC not diagnosed by other tests, and the cost of the test was comparable to other well-established costs.\(^{13,16}\)

The KP Hawaii Region did an analysis of the current well-established bladder tumor markers. A frank malignancy reading for urine cytology (cost, $60.25) had a 41% sensitivity but a 97.2% specificity in 17 studies encompassing 4,685 patients. In four BTA (cost, $98.00) studies encompassing 455 patients, there was a 78% sensitivity and a 80% specificity. In five NMP22 BladderChek Test (cost, $15.50) studies encompassing 846 patients, there was a 80% sensitivity and a 77% specificity. In a study of the FISH test encompassing 456 patients, Sarosdy et al\(^{17}\) found a sensitivity of 68% and a specificity of 80%.

For a clinical test to be useful, it must change what the clinician does. A specificity of 97.2% (2.8% false positive rate) for cytology would likely cause a urologist to have a lower threshold for ordering a biopsy of indeterminate bladder or prostatic urethral lesions and might prompt ureteroscopy.

Recommendation 4

A modified computed tomography (CT) urogram or IVP with concurrent renal ultrasound is recommended for patients with significant hematuria (as already defined). As long as the renal ultrasound is done concurrently with IVP, there is no need for renal tomography. This approach will reduce radiation exposure (Table 3). One caveat: the radiation exposure associated with the modified CT urogram has been reported to be 12 to 24 times higher than with IVP. The modified CT urogram should be conducted with a protocol capable of visualizing any collecting-system lesions using the lowest radiation dose possible. Patients receiving contrast should have a serum estimated glomerular filtration rate (eGFR) test performed before the procedure. When IVP is ordered, clinicians should take into consideration the patient's history of chronic illness (diabetes, heart failure, and other comorbidities), as well as whether the patient takes certain medications (metformin, nonsteroidal anti-inflammatory drugs, and others).

**Evidence review and rationale:** A review of the literature was conducted to identify studies that evaluate the effectiveness of CT urogram and/or IVP for detecting urologic disease. A complementary search of the literature was also conducted to identify studies that compare the relative differences in radiation exposure that may exist between the two imaging modalities. One systematic review and two cohort studies (reports about which were published subsequently to the systematic review) were identified. A brief summary of this evidence is provided below.

One systematic review by Rogers et al\(^{13}\) identified three studies evaluating the use of the CT urogram to

<table>
<thead>
<tr>
<th>Imaging (CPT code)</th>
<th>Millisieverts (msv)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous urogram or intravenous pyelogram (76497)</td>
<td>1.6</td>
</tr>
<tr>
<td>Renal and bladder ultrasound (76175)</td>
<td>0</td>
</tr>
<tr>
<td>KUB (radiograph plain film) (74000)</td>
<td>0.07</td>
</tr>
<tr>
<td>CT without contrast, abdomen and pelvis (74150, 72192)</td>
<td>10</td>
</tr>
<tr>
<td>CT with contrast, abdomen and pelvis (74160, 72193)</td>
<td>14</td>
</tr>
<tr>
<td>CT with and without contrast, abdomen and pelvis (74170, 72194)</td>
<td>24</td>
</tr>
</tbody>
</table>

\(CT = \) computed tomography; CPT = current procedural terminology; KUB = kidneys, ureter, bladder
identify any abnormality that may cause hematuria. According to that review:

One study combined CT with IVP as the reference standard and reported a sensitivity of 100% and a specificity of 97%.

A second study used histopathology as the reference standard and reported a sensitivity of 92% and a specificity of 94%.

A third study evaluated the CT as a method to detect filling defects or strictures in the urinary tract and reported a sensitivity of 82% and a specificity of 97%.

The authors concluded that there is some evidence to support the use of CT to determine the cause of hematuria. However, they also reported that the evidence base is limited evidence to three diagnostic accuracy studies, one of which was poorly reported and not designed for the purpose of detecting significant urologic pathology.

Turney et al. conducted a cohort study (n = 200) comparing CT urogram findings with those for cystoscopy and pathology to determine the diagnostic accuracy of CT urogram (CTU) for detection of bladder cancer. They reported a sensitivity of 93%, a specificity of 98%, a PPV of 98%, and a negative predictive value of 97%. In this publication’s introduction, the study authors claimed that CTU is becoming recognized as the diagnostic tool of choice for many urologic conditions and represents the “gold standard” for examining upper urinary tracts. This explicit bias suggests caution when interpreting the study results.

Another nonrandomized cohort study (n = 512) conducted by Albani et al. examined the diagnostic accuracy of CTU vs IVP in adults with hematuria.

For the identification of upper tract lesions, CTU had a sensitivity of 94% and a PPV of 89%, whereas IVP had a sensitivity of 50% and a PPV of 40%. Owing to the lack of a gold-standard examination for upper tract evaluation, specificity could not be calculated.

For the identification of lower urinary tract lesions, CTU had a sensitivity of 40% and specificity of 93%, whereas IVP had a sensitivity of 37% and a specificity of 97%. Both imaging modalities failed to detect more than 60% of bladder lesions smaller than 2 cm.

The overall detection rates were 25.5% for CTU and 19.4% for IVP.

**Methodologic issues:** The authors identified two cohorts and included in the analysis only those study subjects who could make the required follow-up visits. The effect of this design in reaching definitive conclusions is uncertain.

The authors acknowledged that CTU and IVP were not performed in the same patients and that the increased radiation exposure provided by two tests could not be justified.

The two cohorts were unmatched, but analysis indicated that there were no statistically significant differences in patient characteristics.

Patients were not stratified by risk of disease, and the authors believe that this contributed to the relatively low overall detection rate.

Rogers et al. also identified seven nonrandomized studies evaluating IVP (also known as intravenous urography, or IVU) as an index test for the detection of urologic cancer among people with hematuria. They reported the following results:

“Seven studies evaluated IVU as an index test … . [Four] studies evaluated IVU against final diagnosis, but for different target conditions: upper urinary tract tumors (sensitivity 89%, specificity 95%), lower tract tumors (sensitivity 56%, specificity 98%), any upper tract pathology (sensitivity 67%, specificity 91%), any renal abnormality (sensitivity 90%, specificity 98%) or any filling defect or structure in the urinary tract (sensitivity 68%, specificity 98%). Across the IVU studies, specificity values (range 91%-100%) appeared to be more consistent than sensitivity values (range 55%-90%), although it is difficult to estimate the overall value of IVU as a test owing to the clinical and statistical heterogeneity between studies.”

**Radiation exposure:** Several studies evaluating the radiation exposure levels from CT urogram and IVP among adults with hematuria and flank pain (suspected renal colic) were identified (Kim et al., Homer et al., Thomson et al., and others). The data suggest that radiation may be higher for noncontrast CT (range, 1.4–10.0 millisieverts [mSv]) and noncontrast helical CT (range, 2.806–5.004 mSv) than for IVP (range, 1.48–4.46 mSv). With CT, exposures were consistently higher for women than for men. (Table 3 provides a summary of radiation exposures by imaging test.)

Studies that explicitly evaluated the health impact of different levels of radiation exposure from the CT urogram versus IVP among patients with hematuria were not identified (summary of average doses from American College of Radiology and Radiological Society of North America).

There is no clear consensus that CTU is superior to IVP for a hematuria evaluation; however, there is emerging evidence that this may be the case. Although radiation exposures are higher for CTU than for IVP, newer
CT protocols and technologic advances are reducing radiation dose while increasing the anatomic detail of images in addition to identifying pathology in other organ systems that would not be noted on IVP. The interregional urology chiefs agreed, on a consensus basis, that CTU can be used to evaluate patients with significant hematuria according to a protocol capable of visualizing collecting-system lesions using the lowest radiation dose possible. Patients receiving contrast CT should have a serum creatinine test performed before the procedure. Alternatively, a concurrent IVP and renal ultrasound would also provide acceptable imaging of significant renal masses and collecting-system lesions with less radiation but less standardization (more operator-dependent) (Mariani AJ, personal communication, 2007 May 19).32

The interregional urology chiefs also took the following into consideration:

A CT of the abdomen and pelvis with and without contrast exposes the patient to about 20 times the radiation dose of an IVP. (Note: renal ultrasound has no associated radiation exposure.)

An IVP will detect only 10% of 1-cm lesions and 52% of 2- to 3-cm lesions. Fortunately <4% of renal masses that are <3 cm in size will behave malignant, even though 90% are RCCs. This may be the reason why IVP served urology as well as it did for so long as the standard imaging for a hematuria evaluation.

CT is superior to renal ultrasound for the detection of small renal masses, but renal ultrasound detected 100% of lesions >2.5 cm and the majority of lesions >1.5 cm in one well-designed study.33 Again, most small lesions do not behave malignantly.

Fine-cut CT images can approach the collecting-system detail of an IVP and provide additional functional information. On IVP, tumors present as negative filling defects (as do clots and radiolucent stones). On CT, a tumor will usually opacify after contrast, and a radiolucent stone is easily distinguished from a blood clot. Renal ultrasound can also easily distinguish a clot from a radiolucent stone.

The cost of a CT urogram (~$282) would be approximately the same as the cost of an IVP plus a renal ultrasound (~$228 + ~$87 = ~$315), according to data from KP Hawai Region 2007 (Mariani AJ, personal communication, 2007 May 19).4

CT scans account for 70% of all medical x-ray exposure even though they represent 20% of diagnostic imaging studies. It is estimated that a single dose of 10 mSv (<1 CT scan) has a lifetime cancer risk of 1/1000 and a death rate of 1/2000.

Recommendation 5
There is insufficient evidence to recommend routine UA to screen for asymptomatic hematuria in the absence of clinical indicators.

Evidence review and rationale: Hematuria screening for cancer in the asymptomatic population has not been clinically established. RCTs and high-quality epidemiologic studies supporting the use of routine UA screening among asymptomatic adults are lacking. Furthermore, in a 2006 report, the US Preventive Services Task Force recommended against routine bladder screening among asymptomatic persons.34,35

Routine screening for bladder cancer with urine dipstick, microscopic UA, or urine cytology is not recommended in asymptomatic persons. All patients who smoke tobacco should be routinely counseled to quit smoking.

In patients without significant urologic symptoms, microscopic hematuria is occasionally detected on routine UA. At present, routine screening of adults for microscopic hematuria with UA is not recommended because of the intermittent occurrence of this finding and the low incidence of significant associated urologic disease.

Discussion
Implementation: Collaboration and Tools
Implementation of a nationwide adult asymptomatic microhematuria screening and management program is a result of the collaborative efforts of clinicians representing multiple areas of medical care: urology, primary care, radiology, and laboratory. Many other departments—including guideline development, regional continuing medical education, regional laboratory, and national and regional KP HealthConnect implementation teams—were consulted in both the planning and implementation.

Standardized implementation tools were developed:

- A hematuria-management standardized presentation that is used during chiefs’ Departments of Urology, Primary Care, Radiology, and other meetings to provide an overview of the recommendations and to educate clinicians and staff
- Hematuria practice resource pocket cards to assist clinicians during patient care
- Continuing medical education materials
- KP HealthConnect hematuria diagnosis SmartSet list
- Standardization of reporting of hematuria by laboratory departments
- Implementation and adherence to national practice...
recommendations will be evaluated in the future, and the lessons that this provides will be used to modify practice recommendations, provide feedback to clinicians, and support ongoing performance improvement efforts.

Eliminate One-Quarter of Future Workups

In an effort to minimize variations in reporting and to collect definitive evidence to completely eliminate the need to assess the lowest-risk patients with hematuria in the near future, a KP HealthConnect SmartSet list data collection tool has been developed to allow concurrent electronic data analysis of hematuria workup outcomes. It will be used nationwide by KP urologists to document their workup findings; we estimate that within one year, enough data will be captured to eliminate the need to assess 25% or more of the patients currently being evaluated. A valuable outcome goal is to demonstrate the power and capability of KP HealthConnect in population-based clinical research. To reinforce continuity of care, the KP HealthConnect tool will generate patient-care instructions for further follow-up treatment.

High Radiation Risk

It has been estimated that acute radiation exposures as low as 10 mSv pose significant cancer risk, so much so that a significant number of future cancers will be caused by iatrogenic unnecessary imaging. 26

Conclusions

More than 62 million CT scans are performed annually in the US, a large number of which are due to screening and assessment of asymptomatic patients with microhematuria. Clearly, major efforts to curtail unnecessary radiation exposure are sorely needed. As advocated by the KP IRCUS, an immediate reduction in radiation exposure by collectively switching to a modified CT urogram and a commitment to support the collection of evidence through KP HealthConnect to completely eliminate unnecessary workup underscores our dedication to the KP promise. 27

The KP National Hematuria Guideline has been a tremendous inspiration to all participants. The work illustrates the potential that KP possesses in effecting safer and more reliable evidence-based care as well as its obligation as a health care leader in striving to answer previously unanswerable questions and to change the way that medicine is practiced for our patients and worldwide. 7

Albert J Mariani, MD, Associate Medical Director of Specialty and Hospital Services, Hawaii Permanente Medical Group.

Disclosure Statement

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Acknowledgment

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References


11. Rodgers M, Nixon J, Hempel S, et al. Diagnostic tests and al-


Laparoscopic Surgery for Rectal Cancer

Adrian Indar, MD, MBBS, FRCs, DM
Jonathan Efron, MD, FACS, FASCRS

ABSTRACT

Laparoscopic surgery for rectal cancer is much more challenging than that for colon cancer because of the confined space within the pelvis. Further, because of the tumor’s location in the pelvis, maintenance of resection margins is of greater concern. Nonrandomized studies by groups experienced in laparoscopic surgery have shown both that it produces short-term outcomes equivalent to those for open surgery and that it can be performed safely from an oncologic perspective. Nonsurgical complications appear to be fewer, but conversion to open surgery may become a real issue. This review summarizes these findings by addressing technical considerations, early outcomes, late outcomes, costs, and complications.

INTRODUCTION

Laparoscopic colectomy for malignant disease is widely used and has been readily accepted as being more advantageous than the open approach. Its benefits include less intraoperative blood loss, less postoperative pain, shorter hospital stay, faster return to work, and fewer adhesions. Initial concerns about port-site recurrence and adequacy of the extent of resection have been dismissed.

Laparoscopic surgery (LS) for rectal cancer, however, has not been as universally accepted. We summarize here the short- and long-term results of LS and note some of the technical aspects that influence results.

Surgical resection for rectal cancer mandates at least total mesorectal excision (TME) for middle and low rectal cancers. This procedure regards the rectum and mesorectum as one lymphovascular structure and requires its excision within an intact fascia propria. This has conclusively shown to reduce the rate of local recurrence and increases the rate of survival.

We searched MedLine for the terms laparoscopic surgery and rectal cancer and retrieved 499 publications. Selected articles consisted of meta-analysis, randomized controlled trials, and prospective case series. We considered only English-language articles focusing on rectal cancer only in adults or both colon and rectal cancers in adults where the two groups were considered separately. We excluded articles that commented only on colon cancer or were case reports.

We summarize some of the studies’ results and present the important outcomes in tables in an attempt to standardize these heterogeneous studies. The results are not uniform, so we outline the common trends and raise points of concern that can be addressed by future randomized controlled trials.

TECHNICAL CONSIDERATIONS

Circumferential sharp dissection within the holy plane around the mesorectal package, while maintaining an intact mesorectal fascia and avoiding injury to the nervi erigentes, is fundamental to rectal cancer resection. Because the rectum is closely surrounded by the other pelvic organs and the pelvic side walls, it is imperative to ensure adequate circumferential margins during rectal cancer resection. An involved resection margin is one of the major factors that determine local recurrence and subsequently prognosis. This is avoided by performing adequate preoperative staging, making a proper selection for neoadjuvant therapy, and using meticulous surgical technique with TME, using sharp dissection for cancers in the middle and lower thirds of the rectum.

Acquisition of advanced laparoscopic skills and familiarity with rectal cancer resection are the biggest factors in determining technical success. Male patients have a narrower pelvis than female patients do—and thus visibility and access, though better than with the open technique—are still a challenge. Obese patients frequently require the use of long instruments that are usually reserved for bariatric surgery, and abdominal wall distention may require higher insufflation pressures if possible. An assistant who is similarly competent with the...
Laparoscopic surgery for rectal cancer is invaluable for providing adequate and timely retraction of the rectum, which allows the primary surgeon not to have to switch operating sides. Several series listed in Table 1 and 2 have shown that this is technically possible with the laparoscopic method when done by surgeons who are familiar with pelvic anatomy and have advanced laparoscopic skills.

A high-quality camera with an angled laparoscope is required to provide excellent magnified views of the pelvis, managed by an assistant experienced in laparoscopy. The lack of adequate articulation of endoscopic staplers can be a problem in performing rectal transection at the level of the anorectal ring and could result in an obliquely long stapler line on the anorectal stump, especially in the presence of a bulky tumor in the heavier or male patient. Such situations demand a suprapubic incision in some patients undergoing standard laparoscopic-assisted resection or a mucosectomy with a hand-sewn coloanal anastomosis.

Table 1. Studies showing early outcomes after laparoscopic surgery for rectal cancer

<table>
<thead>
<tr>
<th>Studies</th>
<th>Patients</th>
<th>Preoperative radiotherapy (%)</th>
<th>Conversion (%)</th>
<th>Diversion (%)</th>
<th>Mortality (%)</th>
<th>Morbidity (%)</th>
<th>Leak (%)</th>
<th>Reoperation (%)</th>
<th>Days in hospital (mean)</th>
<th>Blood loss (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hasegawa et al</td>
<td>71 LS</td>
<td>N/A</td>
<td>4.2</td>
<td>30.9</td>
<td>N/A</td>
<td>28.2</td>
<td>13.6</td>
<td>N/A</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>Lelong et al</td>
<td>104 LS vs 68 OS (historic)</td>
<td>78 vs 75</td>
<td>15</td>
<td>93 vs 85</td>
<td>1 vs 3</td>
<td>43.3 vs 48.5</td>
<td>11 vs 20</td>
<td>8.7 vs 7.4</td>
<td>10 vs 14</td>
<td></td>
</tr>
<tr>
<td>Braga et al</td>
<td>83 LS vs 85 OS</td>
<td>16 vs 14</td>
<td>7.2</td>
<td>26.5 vs 24.7 (NS)</td>
<td>1.2 vs 1.2 (NS)</td>
<td>29 vs 40 (NS)</td>
<td>9.6 vs 10.6 (NS)</td>
<td>7.2 vs 12.9 (NS)</td>
<td>10 vs 13</td>
<td></td>
</tr>
<tr>
<td>Staudacher et al</td>
<td>226 LS</td>
<td>48.6</td>
<td>6.1</td>
<td>365.8</td>
<td>0</td>
<td>31.8</td>
<td>16.8</td>
<td>6.6</td>
<td>10.4</td>
<td>203</td>
</tr>
<tr>
<td>Pugliese et al</td>
<td>157 LS; TME in 62%</td>
<td>9.5</td>
<td>7.6</td>
<td>36</td>
<td>1.2</td>
<td>16</td>
<td>10.8</td>
<td>N/A</td>
<td>10.5</td>
<td>N/A</td>
</tr>
<tr>
<td>Rezvani et al</td>
<td>60 LS</td>
<td>13.3</td>
<td>16.6</td>
<td>1.6</td>
<td>16.6</td>
<td>3.2</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ströhlein et al</td>
<td>114 LS vs 275 OS</td>
<td>20.2 vs 14.2 (NS)</td>
<td>21.9</td>
<td>50.6 vs 49.5 (NS)</td>
<td>0</td>
<td>14.0 vs 21.4 (NS)</td>
<td>10.1 vs 15.3 (NS)</td>
<td>15.1 vs 18.7 (Sig)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kim et al</td>
<td>312 LS; 138 EP vs 174 IP</td>
<td>13.8 vs 0.6 (NS)</td>
<td>1.4 vs 3.4 (NS)</td>
<td>42 EP vs 4 IP (Sig)</td>
<td>0.3 EP vs 0 IP (NS)</td>
<td>21.5</td>
<td>6.4; 9.7 EP vs 4.6 IP (NS)</td>
<td>12.7 vs 11.8 (NS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ng et al</td>
<td>51 LS APER vs 48 OS APER</td>
<td>N/A</td>
<td>9.8</td>
<td>N/A</td>
<td>1.9 vs 2.0 (NS)</td>
<td>45.1 vs 52.1 (NS)</td>
<td>N/A</td>
<td>2 vs 8</td>
<td>18.8 vs 11.5 (NS)</td>
<td>321 vs 555</td>
</tr>
<tr>
<td>Laurent et al</td>
<td>200 LS</td>
<td>81.5</td>
<td>15.5</td>
<td>75</td>
<td>1</td>
<td>25</td>
<td>8</td>
<td></td>
<td>9 (4–42)</td>
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<tr>
<td>Tjandra et al</td>
<td>31 LS vs 32 hand assist</td>
<td>25 vs 28 (NS)</td>
<td>0 vs 0 (NS)</td>
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<td>25.8 vs 21.9 (NS)</td>
<td>3 vs 3 (NS)</td>
<td>5.8 vs 5.9 (NS)</td>
<td>152 vs 158 (NS)</td>
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<tr>
<td>Gillou et al</td>
<td>253 laparoscopic assistance vs 128 OS; 25% vs 27% APER</td>
<td>29</td>
<td>4 (9 in converted procedures)</td>
<td>40 vs 37 (NS)</td>
<td>10 vs 7 (NS)</td>
<td>2 more than open</td>
<td></td>
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<tr>
<td>Staudacher et al</td>
<td>108 LS vs 79 OS</td>
<td>63 vs 43 (NS)</td>
<td>12</td>
<td>66 vs 54 (NS)</td>
<td>0%</td>
<td>29.6 vs 27.8 (NS)</td>
<td>14.8 vs 12.6 (NS)</td>
<td>10 vs 12 (NS)</td>
<td>208 vs 356 (Sig)</td>
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<tr>
<td>Rosati et al</td>
<td>20 LS after neoadjuvant therapy vs 26 LS</td>
<td>5 vs 11.5 (NS)</td>
<td>100 vs 15 (NS)</td>
<td>25 vs 35 (NS)</td>
<td>11.1 vs 26.9 (NS)</td>
<td>20 vs 35 (NS)</td>
<td>9 vs 8 (NS)</td>
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</table>

APER = abdominoperineal excision of rectum; DFS = disease-free survival; EP = extraperitoneal; IP = intraperitoneal; LAR = low anterior resection; LS = laparoscopic surgery; NS = not significant; OS = open surgery; Sig = significant; TME = total mesorectal excision.
Early Outcomes

Previous meta-analyses have shown that LS for colorectal cancer is associated with lower morbidity, less pain, a faster recovery, and a shorter hospital stay than is open resection, without compromising oncologic clearance.11 No significant differences in oncologic clearance or lymph node harvesting were identified.11 These two studies failed to exclusively examine data on LS for rectal cancer.

Several prospective case series have shown that LS for rectal cancer is oncologically safe, with early outcomes for mortality, morbidity, anastomotic leak, length of hospital stay, and diversion rate equivalent to those of open surgery (OS)12-15 (in patients whom the operation is completed successfully). Quoted morbidity rates are 11% to 37%.16 Respiratory complications were significantly fewer in one study;7 although this finding has been contradicted by another study.13 Preoperative chemoradiation did not adversely influence rates for anastomotic leaks or overall morbidity (33% vs 23%) in LS when compared with OS.12 Overall, neoadjuvant therapy did not have an adverse effect on early outcome (Table 1).7,17

Conversion rates to OS ranged from 3% to 29%,13,15,18-20 Although high conversion rates can be attributed to surgeon inexperience, progression on the learning curve did not show any significant reduction in conversion rates.21 The most common reasons for conversion were excessive tumor fixity or uncertainty of tumor clearance (41%), obesity (26%), anatomic uncertainty (21%), and inaccessibility of tumors (20%).15 Conversion to OS did not show any difference in postoperative morbidity when compared to procedures that were completed laparoscopically or that were OS from the start.13,22 However, a single study found that conversion was significantly associated with a higher incidence of anastomotic leaks (29%).23 Male sex was a consistent factor associated with conversion to OS.21

Multivariable analysis showed that male sex, a stapled anastomosis, and an intraoperative finding of excess rectal fixity were independent factors for conversion. Further analysis revealed that men with a stapled anastomosis had a threefold higher rate of conversion than all other patients (34% vs 11%; p < 0.001).22

From an oncologic perspective, the percentage of patients having an complete or radical (R0) resection ranged from 82% to 100% among all stages of tumor, regardless of the administration of neoadjuvant therapy.13,19,22 The range of lymph nodes harvested was 12 to 22.23,25,26

A meta-analysis of 10 trials in which the radial margin status was evaluated reported a mean positive radial margin of 5% for laparoscopic resections, compared with 8% for open resections, although this was not statistically significant. The distal margin positivity rates were also not different between LS and OS.7 The distal margin can be of concern in cancers of the lower one-third of the rectum, particularly in men.22

Late Outcomes

A meta-analysis of long-term outcomes of LS for colorectal cancer did examine the subgroup of patients with rectal cancer. It found no significant difference in local recurrence (7.2% vs 7.7%; 95% confidence interval [CI], 0.45-1.43; p = 0.46) or distant metastasis (11.3% vs 13.6%; 95% CI, 0.55-1.22; p = 0.32) between LS and OS for rectal cancer.1

The Medical Research Council Conventional versus Laparoscopic-Assisted Surgery In Colorectal Cancer Trial Group study did show a nonsignificant higher positive circumferential resection margin rate in patients undergoing laparoscopic anterior resection compared with open resection.13 However, this has not translated into any detectable difference in terms of overall survival, disease-free survival, or local recurrence by three-year follow-up examination between the groups.32

No significant difference between LS and OS has been found in both overall five-year survival and disease-free five-year survival.34 A prospective study of 389 patients undergoing either LS or OS for rectal cancer and with a mean follow-up period of 32 months found no difference in survival between the two groups at any stage. The actuarial five-year survivals for LS and OS, respectively, were 85% vs 75% in stage I, 67% vs 73% in stage II, and 60% vs 51% in stage III.13 Probably unrelated to the mode of access, patients with stage III disease who benefited from adjuvant chemotherapy had better survival rates than did those with stage II disease who did not have chemotherapy.25

Reported series comparing LS with OS for rectal cancer found no difference in local recurrences (4% vs 5.2%) at a mean follow-up point of three years; p = .97 and 6.9% vs 9.5% at a mean follow-up point of 32 months; p = .52). There was no difference in rates of neoadjuvant therapy between the groups (Table 1).13,14

A prospective study comparing patients with extraperitoneal rectal cancer vs those with intraperitoneal rectal cancer undergoing LS detected a local recurrence rate at three years of 7.6% for extraperitoneal and 0.7% for intraperitoneal (p = 0.0011).26 Despite a significant difference in the rates of neoadjuvant radiotherapy between the groups, extraperitoneal location of rectal cancers was found, by multivari-
ate analysis, to be a risk factor for recurrence.

Concern was raised in one study about the long-term oncologic outcome for patients whose LS was converted to OS. Twenty-six percent of a cohort of patients undergoing converted, curative surgery were found, at follow-up examination, to have metachronous metastasis. Their local recurrence rate was 16%.13 These increased rates indicate the problems with conversion in LS for cancer. Conversion frequently occurs too late in the operation, after the surgeon has spent significant time with little progress or tries to correct surgi-

<table>
<thead>
<tr>
<th>Studies</th>
<th>Patients</th>
<th>R0 resection (%)</th>
<th>No. of nodes</th>
<th>Margin (mm)</th>
<th>Mean follow-up duration (months)</th>
<th>Local recurrence (%)</th>
<th>METs (%)</th>
<th>Port-site METs (%)</th>
<th>Five-year overall survival</th>
<th>Five-year DFS</th>
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<tbody>
<tr>
<td>Lelong et al17</td>
<td>104 LS vs 68 OS (historic)</td>
<td>9.7 vs 18</td>
<td>11 vs 9</td>
<td>21 vs 31</td>
<td>33</td>
<td>4–7.6 EP vs 0.7 IP (Sig)</td>
<td>13.3 EP vs 12.4 IP</td>
<td>0</td>
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<tr>
<td>Kim et al16</td>
<td>312 LS; EP (138) IP (174)</td>
<td>91.3 EP vs 99.2 IP (Sig)</td>
<td>22 vs 24 (NS)</td>
<td>21 vs 34 (NS)</td>
<td>33</td>
<td></td>
<td>0</td>
<td>0</td>
<td>Probability 75.2% vs 76.5%</td>
<td>Probability 78.1% vs 73.6%</td>
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<tr>
<td>Ng et al11</td>
<td>51 LS APER vs 48 OS et al</td>
<td>94 vs 96 (NS)</td>
<td>12.4 vs 13 (NS)</td>
<td>87 vs 90</td>
<td>5 vs 11</td>
<td>0</td>
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<td>Probability 75.2% vs 76.5%</td>
<td>Probability 78.1% vs 73.6%</td>
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<td>Tjandra et al9</td>
<td>31 pts LS vs 32 with hand assist</td>
<td>3.2 vs 3.1 (NS)</td>
<td>17 vs 17 (NS)</td>
<td>26 vs 26 (NS)</td>
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<td>0</td>
<td>0</td>
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<tr>
<td>Gillou et al,15, Jayne et al12</td>
<td>253 laparoscopic assistance vs 128 OS; 25 vs 27% APER</td>
<td>84 vs 86 (NS)</td>
<td>13.5 vs 12 (NS)</td>
<td>36</td>
<td>9.7 vs 10.1 (NS)</td>
<td>18.6 vs 16 (NS)</td>
<td>1.7 vs 0.03 (NS)</td>
<td>3-year survival 74.6% vs 66.7% for patients with anterior resection</td>
<td>3-year survival 70.9% vs 70.4% for patients having anterior resection</td>
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<tr>
<td>Staudacher et al10</td>
<td>226 LS; 202 LAR, 24 APER</td>
<td>97.4</td>
<td>14.4</td>
<td>27</td>
<td>40</td>
<td>6.1</td>
<td>Cumulative survival: 81%</td>
<td>70%</td>
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<tr>
<td>Staudacher et al12</td>
<td>108 LS vs 79 OS</td>
<td>14.3 vs 15.2</td>
<td>24 vs 27</td>
<td>27</td>
<td>6.4 vs 5</td>
<td>14.8 vs 18.9 (NS)</td>
<td>1 vs 0</td>
<td>Stage II: 85.4% vs 75.2%; stage II 66.7% vs 73.4%; stage III 60.1% vs 51.3% (NS)</td>
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<tr>
<td>Ströhlein et al11</td>
<td>114 LS vs 275 OS</td>
<td>96 vs 95</td>
<td>13.5 vs 16.4</td>
<td>31</td>
<td>6.9 vs 9.5, 16 in converted procedures</td>
<td>17.8 vs 14.9</td>
<td>1 vs 0</td>
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<tr>
<td>Lee et al13</td>
<td>497 LS; All T3</td>
<td>N/A</td>
<td>18</td>
<td>31</td>
<td>Estimated 5 year (9.4%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Laurent et al22</td>
<td>200 LS</td>
<td>87.5</td>
<td>11</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Bianchi et al14</td>
<td>107 LS</td>
<td>98</td>
<td>18</td>
<td>26</td>
<td>36</td>
<td>1</td>
<td>0</td>
<td>Actuarial survival 81.4%</td>
<td>Actuarial survival 79.8%</td>
<td></td>
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<tr>
<td>Pugliese et al21</td>
<td>157 LS; TME in 62%</td>
<td>N/A</td>
<td>12</td>
<td>48</td>
<td>39</td>
<td>4</td>
<td>11</td>
<td>Cumulative probability 0.73%</td>
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<tr>
<td>Braga et al14</td>
<td>83 LS vs 85 OS</td>
<td>98.9 vs 97.6 (NS)</td>
<td>0 vs 0</td>
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<td></td>
<td></td>
<td>0.7</td>
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<tr>
<td>Rosati et al18</td>
<td>20 LS after neoadjuvant therapy vs 26 LS</td>
<td>100 vs 100 (NS)</td>
<td>13 vs 21 (NS)</td>
<td>10 vs 16 (NS)</td>
<td></td>
<td></td>
<td>0.7</td>
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APER = abdominoperineal excision of rectum; DFS = disease-free survival; EP = extraperitoneal; IP = intraperitoneal; LAR = low anterior resection; LS = laparoscopic surgery; MET = metabolic equivalent; NS = not significant; OS = open surgery; R0 = complete/radical; Sig = significant; TME = total mesorectal excision.
cal complications laparoscopically without success. The decision to convert should be seen as a good surgical decision rather than a failed operation.

**Costs and Complications**

The lack of widespread use of LS for colorectal cancer may be related to the associated increase in operating time, cost, and learning curve.

In a single-center randomized study to assess the difference in costs between LS and OS for rectal cancer, the extra operating room charges in the LS group were $1748 per patient (surgical instruments, $1194; longer room occupancy, $554). In patients with an uneventful postoperative course, the mean cost of routine care in the LS group (mean length of hospital stay, 8.6 days) and in the OS group (mean length of hospital stay, 10.4 days) translated in savings of $647 per patient randomized to the LS group. The additional cost of postoperative complications resulted in savings of $749 per patient randomized to the LS group. The overall savings per patient randomized to the LS group were $1396. Considering the additional OR charges in the LS group, there was $351 extra cost per patient.

The late complication rate in this study was 2.4% in the LS group, compared with 10.6% in the OS group (p = 0.07). Quality of life was significantly better in the LS group, but only in the first year after surgery.

Sexual and urinary function were reported in two studies. Patients with T3 lower rectal cancer treated by preoperative chemoradiation underwent laparoscopic sphincter-saving TME, preserving the pelvic autonomic nerves. Seventy-four patients with normal preoperative sexual function were evaluated when the temporary colostomy had been closed and the patients were completely recovered. The voiding function was good in 72%, fair in 23%, and poor in 5%. Of the 17 patients with fair bladder function, 8 had transient function. In 32 male patients, ejaculation was good in 56%, fair in 19%, and poor in 25%, whereas potency was good in 62% of patients, fair in 16%, and poor in 22%. In 28 female patients, sexual function was reported as good in 54%, fair in 14%, and poor in 32%.

The second study that reported on patients undergoing laparoscopic (n = 34) or open (n = 29) TME between 2002 and 2006 found that LS for rectal cancer offers a significant advantage with regard to preservation of postoperative subjective sexual function in comparison to preoperative function. Postoperatively, only minor disturbances of bladder function were seen in 3% in LS and in 9% in OS (p > .05). Impotence after surgery in males who were sexually active before surgery was experienced by 5% who underwent LS and by 29% who underwent OS (p = .04). Similarly, 7% of women in the LS group and 50% in the OS group reported that their overall level of sexual function had decreased as a result of surgery (p = 0.03). The proposed advantages have been attributed to improvement in visibility in LS.

**Conclusion**

Randomized controlled trials have shown that LS for rectal cancer is equivalent to OS in early outcomes, and in long-term outcomes on nonrandomized cohorts. Laparoscopic TME is technically feasible in the vast majority of patients with lower rectal cancer regardless of whether they have undergone chemoradiation therapy. Surgically, there are some aspects of the laparoscopic technique, such as access and visibility of the distal rectum in the depth of the pelvis, that are superior to those of the open method. Ultimately, the verdict on this surgery will await the outcome of two large multicenter, randomized, controlled trials (in Europe and North America) that are presently recruiting surgeons experienced in this technique to conclusively evaluate the overall status of LS for rectal cancer.

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**Disclosure Statement**

The author(s) have no conflicts of interest to disclose.

**Acknowledgment**

Katharine O’Moore-Klopf, ELS, of KOK Edit provided editorial assistance.

**References**

7. Akasu T, Takawa M, Yamamoto S, Fujita S, Moriya Y. Incidence and patterns of recurrence after intersphincteric resection for very low rectal
Laparoscopic Surgery for Rectal Cancer


A Case of Large Pericardial and Pleural Effusions Associated With Pulmonary Emboli in a User of Crack Cocaine

**Abstract**

We submit here an unusual case in which a user of crack cocaine presented with progressive dyspnea of subacute duration and was subsequently found to have concurrent pericardial and pleural effusions and pulmonary emboli. To our knowledge, there is only one prior case report that describes a potential causal relationship between crack cocaine and the development of a pleural effusion, via an eosinophilic process. In contrast in our patient, the most probable mechanism is that crack cocaine induced a prothrombotic state that promoted formation of pulmonary emboli, which are known to be directly associated with exudative pleural or pericardial effusions. An alternative hypothesis is that sympathetic activation or neurostimulation, which is mediated through release of adrenergic neurotransmitters by cocaine, may cause inflammatory changes in the pleura or pericardium. Finally, the pericardial effusion, pleural effusion, and pulmonary emboli could be concurrent but independent processes.

**Case History**

A man, age 56 years, who had undergone a partial colectomy for a benign polyp in the past presented to the Emergency Department (ED), reporting three months of progressive dyspnea on exertion with routine daily activities. He said that he had no chest pain, upper respiratory symptoms, hemoptysis, fever, weight loss, or other constitutional symptoms. The patient acknowledged using crack cocaine on the day before his presentation, and at least once weekly for the preceding four months. There was no history of chest trauma. His blood counts, metabolic panel findings, cardiac enzymes, and B-type natriuretic peptide levels were normal, and his D-dimer level was elevated. An electrocardiogram revealed low voltage with sinus tachycardia, rate of 106 beats per minute, and no ischemic changes. Chest radiography revealed cardiomegaly and bilateral pleural effusions. Chest computed tomography confirmed large pericardial and bilateral pleural effusions. Chest computed tomography confirmed large pericardial and bilateral pleural effusions, with compressive atelectasis and pulmonary emboli in the left lower lobe. Emergency echocardiography revealed free-flowing pericardial effusion without tamponade, and a normal ejection fraction. Serology for HIV, antinuclear antibody, rheumatoid factor, hepatitis, and thyroid were all normal, as were findings for hypercoagulability. Concurrent thoracotomy with drainage of the pleural effusion and a pericardial window for the pericardial effusion were performed. During the procedures, 1500 mL of serosanguineous fluid was evacuated from the pericardial space and another 1500 mL from the pleural space. The fluid analysis was consistent with an exudative process, with a lactate dehydrogenase of >4000 U/L. Eosinophilia was not observed in the effusions. Gram stains for bacteria and acid-fast bacilli produced normal findings. Pericardial and pleural biopsies demonstrated chronic inflammation, but no malignant changes. An infrarenal vena cava filter was placed, and interval radiographs revealed complete resolution of the effusions. The patient was discharged to home.

**Discussion**

To our knowledge, crack cocaine abuse in association with concurrent pericardial and pulmonary effusions has not been previously reported. The most probable link between the crack cocaine use and the effusions are the pulmonary emboli. Cocaine is known to induce a prothrombotic state that may lead to pulmonary emboli, which are known to be as-

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**Connie Le, MD**

**Hanh Nguyen, MD**
CASE STUDY

A Case of Large Pericardial and Pleural Effusions Associated With Pulmonary Emboli in a User of Crack Cocaine

Accordingly, associated with pericardial or pleural effusions. Alternatively, cocaine may cause direct cardiac and pulmonary toxicity. It is also speculated that sympathetic nervous system activation and release of adrenergic neurotransmitters by cocaine may lead to inflammatory changes in the pleural or pericardial surfaces in a hypothetical process of neuro-stimulation.

Epidemiology
Cocaine is the second most commonly used illicit drug in the US, which is the world’s foremost consumer of this drug. An estimated 1.5 million Americans use cocaine regularly, defined as use at least once monthly. Approximately 25% of patients ages 18 to 45 presenting with chest pain to the ED admit to cocaine use.

Pharmacology
Cocaine is derived from the erythroxylone coca plant and historically has had medicinal uses, including as a local anaesthetic and as a treatment for depression. Cocaine stimulates the sympathetic nervous system by blocking reuptake of catecholamines, including norepinephrine, epinephrine, and dopamine at the presynaptic receptors. Excess catecholamines at postsynaptic receptors activate the sympathetic system, and clinical manifestations include tachycardia, hypertension, vasoconstriction, and hyperthermia.

Cocaine and Cardiac and Pulmonary Toxicity
Cardiovascular complications associated with cocaine abuse include myocardial ischemia, myocarditis, cardiomyopathy, and aortic dissection. These effects can be explained in terms of cocaine’s pharmacologic effects. Elevations in heart rate, blood pressure, and afterload lead to increased myocardial oxygen demand in the face of concomitant reductions in coronary blood flow and cardiac contractility induced by cocaine.

Pulmonary complications associated with crack cocaine inhalation include asthma, eosinophilic pneumonia, bronchiolitis obliterans and organizing pneumonia, pneumothorax, and pneumomediastinum.

General Etiology and Mechanisms of Formation of Pericardial and Pleural Effusions
A brief schematic differential diagnosis of pericardial effusions
includes infections (coxsackievirus A and B, hepatitis, HIV, pneumococci, streptococci, staphylococci, tuberculous, fungal, syphilitic, protozoal, parasitic); idiopathic disorders; uremia; neoplasms, including primary tumors such as mesothelioma and tumors metastatic to the pericardium; myocardial infarction and aortic dissection with leakage into the pericardial sac; collagen vascular diseases (systemic lupus erythematosus, rheumatoid arthritis, ankylosing spondylitis, scleroderma), trauma, and drug-induced (procainamide, hydralazine, isoniazid, minoxidil, phenytoin, anticoagulants, methysyngide) disorders. These different etiologies also account for most cases of pleural effusions. 

In general, the mechanism of the accumulation of pericardial fluid accumulation is injury or inflammation of the pericardium. Transudative fluids arise from obstruction of lymphatic channels, and exudative fluids occur from inflammatory, infectious, or autoimmune processes within the pericardium.

In general, pleural effusions result from disturbances in normal pleural fluid transport. There are three main mechanisms behind the disturbances—abnormalities in Starling equilibrium, increased capillary and mesothelial permeability, and obstruction of lymphatic drainage. 

Cocaine and Thrombosis

The clinical finding of pulmonary embolus in the patient under discussion here may be explained in terms of the prothrombotic effects of cocaine. The drug promotes platelet aggregation and activation and enhanced production of thromboxane and plasminogen activator inhibitor, leading to thrombosis at sites of intense vasospasm. 

### Pulmonary Embolus as the Link Between Cocaine and Pleural Effusion

The patient under discussion in the prior case by Strong and colleagues uses crack cocaine and has pleural effusion. It was these authors’ contention that there was a causal relationship between the two, through an eosinophilic process. An eosinophilic pleural effusion was observed in this patient that mimicked an empyema, and glucocorticoids led to prompt resolution of the effusion. Inflammatory cytokines, including interleukin-5 (IL-5), IL-6, and IL-8, and a leak-mediating vascular endothelial growth factor were implicated. 

Like the patient whose case was reported by Strong and colleagues, our patient had an exudative effusion, determined on the basis of Light’s criteria. However, hypereosinophilia was not present in either serum or the effusions. In the most recently reported case series, pulmonary embolism was associated with exudative pleural effusions in 30% of patients and tended to be small, unilateral, and on the ipsilateral side of the emboli. The case reported here is different in that the effusions were large and bilateral. Restriction of cardiac contractility by the large pericardial effusion might also have promoted development of the bilateral pleural effusions. 

**Cardiac Toxicity and Pericardial Effusions Induced by Drugs and Pulmonary Emboli**

Large pericardial and pleural effusions have been reported in association with chemotherapeutic agents such as carmustine (BCNU), an alkylating agent that causes cardiopulmonary toxicity. Early use of glucocorticoids significantly reduced the BCNU-related pleural-pericardial toxicity. Large pericardial effusions have been described in conjunction with pulmonary emboli, and timely insertion of catheters for their drainage was recommended because of the high probability of cardiac tamponade. 

It is possible that cocaine is related more than temporally to the pericardial and pleural effusions in our patient. One potential mechanism is that cocaine may promote development of the pulmonary emboli, which subsequently cause a pleural-pericardial syndrome. Another alternative is that cocaine may cause direct toxicity similar to that caused by the chemotherapeutic drug just described.

An alternate, albeit speculative, theory of neurostimulation contends that a variety of physiologic and systemic stressors lead to an activation of the sympathetic nervous system with release of stress hormones, catecholamines, and renin. Acute or repeated physiological stress by cocaine, and mediated by catecholamines and neuro-hormonal factors, may produce acute or chronic inflammatory changes in the pericardium. Interestingly, minoxidil is a drug that is associated with pericardial and pleural effusions, and it shares a common pharmacology with cocaine, which is reflex activation of the sympathetic system and renin-angiotensin system. More studies should be performed to better elicit the pharmacology of drug-induced pericardial effusions, as multiple mechanisms are likely, owing to the diverse categories of drugs that are involved. However, it could be possible that the pulmonary emboli
and pericardial and pleural effusions arose through independent processes in this patient whose case is discussed here.

**Conclusion**

Our patient had concurrent pericardial and pleural effusions and pulmonary emboli associated with crack cocaine abuse. This case illustrates the broad differential diagnosis that the clinician must have when evaluating a patient with cocaine-induced chest pain or dyspnea.

**Disclosure Statement**
The author(s) have no conflicts of interest to disclose.

**Acknowledgment**
Katharine O’Moore-Klopf, ELS, of KOK Edit provided editorial assistance.

**References**

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**Less Barbaric**

The local manufacture of catgut from ox peritoneum, the distillation of alcohol, our main antiseptic, from rice, and the spinal use of cocaine as an anaesthetic helped to make surgery less barbaric than it might have been.

—Alfred E Coates, Medical Journal of Australia. 1946
CASE STUDY

Recognition of Kawasaki Disease

Abstract

Kawasaki disease is one of the most common vasculitides of childhood. It is the leading cause of acquired heart disease in children in the US. Although its course is typically self-limited, it is important that the clinician have a high degree of suspicion for its presence in light of its potential cardiac complications. It should be included in the differential diagnosis for any child with prolonged fever that is unresponsive to antibiotics. Diagnosis is often difficult in that the symptoms tend to present at different times. Usually a detailed medical history and multiple examinations (on different days) are needed to establish the diagnosis. Here, we present the case of a boy in whom a delayed diagnosis of Kawasaki disease was made after he had made multiple visits to pediatricians and also to the Emergency Department. In addition, the diagnostic criteria, differential diagnosis, treatment, and possible complications of Kawasaki disease are reviewed here.

Introduction

Kawasaki disease is a generalized vasculitis that affects medium-size arteries. It is characterized by systemic inflammation that manifests as persistent fever, erythema of the mucous membranes, bilateral nonexudative conjunctivitis, rash, swelling and redness of the hands and feet, and cervical lymphadenopathy. Diagnosis is made difficult by the fact that these symptoms are not usually all present at the same time; the only persistent symptom is fever. Therefore, repeated examinations usually occur before a diagnosis of Kawasaki disease is made. Ninety percent of cases involve children younger than five years, with the average age of patients being two years. The disease is relatively uncommon in children younger than six months. Boys are affected about 50% more often than girls are. The disease occurs year round, but cases tend to cluster in the winter and spring. The annual incidence of Kawasaki disease in the US is 17 to 18 children per 100,000. The incidence is greatest in those with Asian ancestry.

The disease tends to be self-limiting and usually resolves without treatment within about 12 days. However, serious cardiac complications can occur, such as coronary artery aneurysms, decreased myocardial contractility, congestive heart failure (CHF), arrhythmias, and myocardial ischemia. Early recognition and treatment significantly reduces the incidence of these complications. Without treatment, 20% to 25% of patients develop cardiac complications; with treatment, the incidence decreases to 4%. Treatment should be initiated as soon as the diagnosis is made and should involve the administration of intravenous immunoglobulin (IVIG) and high-dose aspirin.

Case Study

A previously healthy boy, age 11 years, was seen in both the clinic and the Emergency Department a total of 5 times during a 13-day period for symptoms that included persistent fevers of up to 40º C [104° F], vomiting, diarrhea, headache, cough, sore throat, and rash. The rash was erythematous and initially appeared on his groin and upper thighs. It eventually spread to involve most of his torso, thighs, and upper arms; the skin in the involved areas later began to peel. The boy also developed redness and swelling on the palms of his hands and soles of his feet. His presentation differed at each examination, with the only consistent symptom being high fevers. No laboratory tests were done except for a throat culture, which produced negative findings. It was not until his fifth visit 13 days after initial presentation that Kawasaki disease was suspected. At that point, the patient reported ongoing fevers, vomiting, diarrhea, ear pain, and rash. The skin on his distal fingertips had begun to blister and peel in sheets. His lips were dry and cracked, and he had tender, right-sided cervical lymphadenopathy. It was also noted that he had lost approximately 7 kg since his initial visit 13 days earlier. Laboratory tests done at the time produced normal findings except for the following: erythrocyte sedimentation rate (ESR), 107 mm/h; C-reactive protein (CRP) level, 98 mg/L; hemoglobin level, 11.1 mg/dL;
sodium level, 132 mEq/L; potassium level, 3.3 mEq/L; antistreptolysin O titer, >1500 Todd units/mL.

The boy was then hospitalized and treated with IVIG and high-dose aspirin. An echocardiogram produced normal findings. By the following morning, his symptoms and appearance had improved, and within two days, he was afebrile. He was then discharged from the hospital and instructed to take aspirin for six weeks. A follow-up echocardiogram done six weeks after discharge showed normal coronary arteries, and repeat ESRs gradually trended down to near normal over the two month period following discharge.

**Discussion**

**Diagnosis**

The symptoms of Kawasaki disease are representative of systemic inflammation. It is important to realize that often not all of the symptoms are present at the same time, so repeated examinations may be necessary before a diagnosis can be made. Diagnosis requires the presence of persistent, unexplained fevers for at least five days. Fevers are usually high (often 40° C [104° F] or higher) and are unresponsive to antipyretics and minimally responsive to antibiotics and antipyretics. Four or more of the following symptoms must also be present (Table 1):

- Mucous membrane changes, including red, swollen, cracked lips and strawberry tongue, are commonly present in patients with either typical or with incomplete Kawasaki disease [discussed under the heading “Incomplete (Atypical) Kawasaki Disease”].
- Oral mucosa changes, including red or cracked lips, pharyngeal erythema, or strawberry tongue
- Bilateral nonexudative conjunctivitis, sparing the limbus
- Cervical lymphadenopathy, usually unilateral, with one node ≥1.5 cm in size
- Polymorphous rash
- Extremity changes (erythema of palms and soles, swelling of hands and feet, periungual desquamation in the convalescent phase)

**Laboratory Tests**

The diagnosis of Kawasaki disease is clinical, and there are no confirmatory laboratory tests. However, certain laboratory findings can be used to support the diagnosis, which include those listed in Table 2 and the following:

- Thrombocytosis, which usually occurs around the second to third week of illness, with an average value of 700,000/mm³
- Moderate elevation of transaminase levels, which occurs in 30% of patients (due to hepatic congestion)
- Abnormal serum lipid levels, including elevated triglyceride levels and low-density lipoprotein levels and decreased high-density lipoprotein levels. These can take years to return to normal if the patient is not treated with IVIG
- Hyponatremia (sodium levels <135 mEq/L), is associated with an increased risk of coronary artery aneurysms.

### Table 1. Diagnostic criteria for Kawasaki disease

**Diagnosis requires unexplained fever for ≥5 days in addition to the presence of ≥4 of the following:**

- Oral mucosa changes, including red or cracked lips, pharyngeal erythema, or strawberry tongue
- Bilateral nonexudative conjunctivitis, sparing the limbus
- Cervical lymphadenopathy, usually unilateral, with one node ≥1.5 cm in size
- Polymorphous rash
- Extremity changes (erythema of palms and soles, swelling of hands and feet, periungual desquamation in the convalescent phase)

### Table 2. Laboratory findings suggestive of Kawasaki disease

- Elevated erythrocyte sedimentation rate (≥40 mm/h) or C-reactive protein level (≥3.0 mg/L)
- White blood cell count ≥15,000/μL
- Normochromic, normocytic anemia for age
- Sterile pyuria (≥10 white blood cells per high-power field)
- Serum alanine aminotransferase level >50 U/L
- Serum albumin level ≤3.0 mg
- Platelet count ≥450,000/mm³ after seven days of illness
Recognition of Kawasaki Disease

**Echocardiography**
An echocardiogram should be obtained at the time of diagnosis in all patients with typical or incomplete Kawasaki disease to look for cardiac complications. A repeat echocardiogram should be done six to eight weeks after disease onset to confirm the efficacy of treatment.

**Disease Course**
The course of Kawasaki disease tends to be self-limited, with symptoms lasting an average of 12 days without treatment. It consists of three phases:
- **Acute febrile phase:** This is the phase during which most symptoms occur. It tends to last 7 to 14 days.
- **Subacute phase:** This lasts from the end of the fever until approximately day 25. This is the phase during which desquamation, arthritis, and arthralgias usually occur. Elevated platelet counts are also commonly seen during this phase.
- **Convalescent phase:** This covers the period from when clinical signs disappear until the acute-phase reactants (eg, ESR) return to normal. The average duration is six to eight weeks after the onset of illness.

**Complications**
As already mentioned, cardiac complications can occur in 20% to 25% of untreated patients and in 4% of treated patients. The most common cardiac complication seen in Kawasaki disease is coronary artery aneurysm; however, other cardiac sequelae can occur, including decreased myocardial contractility, congestive heart failure, arrhythmias, pericarditis, pericardial effusion, and myocardial ischemia. It has surpassed rheumatic fever as the most common cause of acquired heart disease in children. Mortality from cardiovascular complications in Kawasaki disease is approximately 0.1% to 2%.

Coronary artery aneurysms usually become apparent 1 to 3 weeks after the onset of fever; appearance more than 5 weeks after fever onset is uncommon. They tend to resolve in 50% of patients within 5 to 18 months. Expedient diagnosis is important because treatment with IVIG within the first 10 days of illness produces a fivefold reduction in the incidence of coronary artery aneurysms.

Certain patient characteristics appear to be related to an increased risk of developing coronary artery aneurysms:
- **Age <1 year or >6 years (because of delayed diagnosis)**
- **Male sex**
- **Fever for >14 days**
- **Serum sodium level <135 mEq/L**
- **Hematocrit <35%**
- **White blood cell count >12,000/μL.**

Cardiovascular complications can be prominent in the acute phase and are the leading cause of morbidity and mortality in Kawasaki disease. Decreased contractility can occur in the acute phase, and it occasionally progresses to CHF. However, normal contractility is usually restored after treatment with IVIG. Patients are unlikely to develop clinically significant cardiac dysfunction after the fevers have resolved.

Myocardial infarction (MI) can occur during the acute phase but is more likely to occur one year or even several years later, especially in patients with giant aneurysms (ie, those >8 mm in diameter). Symptoms of MI in children include inconstant crying, vomiting, stomach upset, and shock. The majority of these infarcts occur during sleep or rest.

Patients younger than one year appear to be at the greatest risk of developing cardiovascular complications, possibly because of delayed diagnosis. Therefore it is important to have a high degree of suspicion for the disease regarding children of all ages who appear with prolonged, unexplained fevers.

**Incomplete (Atypical) Kawasaki Disease**
Patients may be found to have incomplete Kawasaki disease if they exhibit fever and some of the classic symptoms but not enough to meet the diagnostic criteria (ie, fewer than four of the five principal clinical findings). Ten percent of children who develop coronary artery aneurysms fall into this category. Infants, especially those younger than six months, are especially likely to have an incomplete presentation. The finding most consistently absent in incomplete Kawasaki disease is cervical lymphadenopathy (present in only 10%). Rash is absent in 50%, and extremity changes are absent in 40%. Mucous membrane changes are the most consistent finding.

Laboratory evaluation is recommended for the following:
- **Patients younger than six months with unexplained fever for ≥7 days, even if they exhibit none of the classic symptoms of Kawasaki disease**
- **Patients of any age with unexplained fever for ≥5 days who exhibit three or fewer of the classic symptoms**
- **Laboratory evaluation should include:** complete blood cell count, ESR, CRP level, urinalysis, alanine aminotransferase level, and albumin level.
Differential Diagnosis

Kawasaki disease can closely mimic other syndromes and infections (Table 3). It is commonly misdiagnosed as a viral exanthem. Symptoms that point to a diagnosis other than Kawasaki disease include exudative conjunctivitis, exudative pharyngitis, generalized (rather than cervical) lymphadenopathy, discrete intraoral lesions, and a bullous or vesicular rash.

Toxin-mediated illnesses, such as group A streptococcus infections (eg, toxic shock syndrome and scarlet fever) can also present with fever, rash, mucous membrane changes, and abnormal extremity findings. Desquamation in Kawasaki disease tends to affect the hands and feet, as it does in toxic shock syndrome; however, in Kawasaki disease, it usually begins in the periungual region. In scarlet fever, the desquamation tends to be diffuse and flaking, whereas in Kawasaki disease it tends to be sheetlike. Toxin-mediated illnesses generally lack the articular involvement.

Measles, echovirus, adenovirus, and Epstein-Barr viral infections can also mimic Kawasaki disease; however, these conditions usually lack the signs of systemic inflammation as well as the extremity changes seen in Kawasaki disease. Another condition that can be mistaken for Kawasaki syndrome is acrodynia (mercury hypersensitivity reaction). This also presents with fever, rash, swelling of the hands and feet, desquamation, and photophobia. However, this is relatively rare and is a much less likely diagnosis unless there is a convincing history of mercury exposure.

Although the patient described in the case study was somewhat atypical regarding age, his symptoms were highly suggestive of Kawasaki disease. Swelling of the palms and soles as well as periungual desquamation are very typical for Kawasaki disease. The elevated ESR and CRP levels also support the diagnosis, as does the rapid improvement in symptoms after the initiation of treatment.

Etiology

The cause of Kawasaki disease is unknown. Data support the idea of an infectious etiology; however, no one particular virus or bacteria has been implicated. There are circumstantial data supporting the role of

| Table 3. Differential diagnosis of Kawasaki disease<sup>5</sup> |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Indications** | **Kawasaki disease** | **Stevens-Johnson syndrome** | **Streptococcal scarlet fever** | **Toxic shock syndrome** | **Systemic juvenile rheumatoid arthritis** |
| Age (years) | Usually <5 | Any age | Usually 2–8 | Usually >10 | 2–5 |
| Fever | Persistent | Prolonged | Variable, usually <10 d | Usually <10 d | Prolonged |
| Eyes | Nonexudative conjunctivitis, limbal sparing | Exudative conjunctivitis, keratitis | Normal | Conjunctivitis | Normal |
| Oral mucosa | Diffuse erythema, strawberry tongue | Erythema, ulceration, pseudomembrane formation | Pharyngitis, strawberry tongue | Erythematous | Normal |
| Extremities | Erythema of palms and soles, indurative edema, periungual desquamation (tends to be sheetlike) | Normal | Flaky desquamation | Swelling of hands and feet | Arthritis |
| Rash | Erythematous, polymorphous; targetoid or purpuric | Target lesions | Sandpaper rash, Pastia sign, circumoral pallor | Erythroderma | Transient, salmon pink |
| Cervical lymphadenopathy | At least one lymph node ≥1.5 cm | Normal | Paintful swelling | Normal | Diffuse adenopathy |
| Characteristic lab results | Systemic inflammation, anemia, transaminitis, thrombocytosis after day 7 | Associated herpes virus infection | Positive throat culture | Thrombocytopenia | Systemic inflammation, anemia |
| Other | Arthritis | Arthralgia, associated herpes virus infection (30%–75%) | Throat culture positive for group A streptococcus | Mental status changes, coagulopathy, shock | Pericarditis |

Recognition of Kawasaki Disease

some bacterial toxins (eg, staphylococcal toxic shock toxin, streptococcal erythrogenic toxin) and viruses (Epstein-Barr virus, parvovirus, HIV-2); however, these data have not been substantiated. Evidence in support of an infectious etiology includes seasonal distribution, age of affected persons, and the fact that the disease often occurs in epidemics. As the condition is more frequently found in those with Asian ancestry, it is likely that genetic factors play a role as well.

Treatment

Treatment should begin with IVIG and high-dose aspirin as soon as the diagnosis is made. The recommended dose of IVIG is 2 g/kg given as a one-time infusion during an 8- to 12-hour period. It is recommended that this be given within the first 10 days of illness, the point before which aneurysms typically develop. The exact mechanism of action of IVIG is unknown, but it appears to have generalized anti-inflammatory properties. In addition to prevention of coronary artery aneurysms, it also appears to help normalize lipid profiles and improve cardiac contractility.

The patient should also be given aspirin for its anti-inflammatory and antiplatelet activity. This should be given as 80 to 100 mg/kg per day, divided into 4 doses. This dosage should be continued until the child has been afebrile for 48 hours. The dose should then be decreased to 3 to 5 mg/kg per day. This lower dose should be continued until laboratory markers (eg, ESR, platelet counts) return to normal, unless coronary artery aneurysms are present.

Prognosis

The overall prognosis for patients with Kawasaki disease is dependent on the severity of coronary artery involvement as a risk factor for myocardial ischemia. Patients with aneurysms larger than 8 mm are at highest risk for MI. Aneurysms that are 8 mm or smaller tend to regress over time, and those that are 6 mm or smaller tend to resolve completely. Patients without any cardiovascular abnormalities tend to do well and are generally asymptomatic at their long-term follow-up examination.

Conclusion

Kawasaki disease is a common vasculitis of childhood that presents with unexplained fevers for more than five days, rash, oral mucous membrane changes, conjunctivitis, cervical lymphadenopathy, and peripheral extremity changes. Because all of the symptoms are rarely present together at the same time, the diagnosis can be difficult to make, and the clinician must have a high degree of suspicion for the disease. Kawasaki disease should be included in the differential diagnosis for any child with a prolonged unexplained fever, and the appropriate medical history questions should be asked.

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References

Part 1: Barriers, Solutions, and Motivation

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Introduction
Five Case Examples
1. AJ, a woman, age 57 years, was diagnosed with hypertension and given a prescription for Lisinopril. After one week, she stopped taking the medicine because she was too dizzy to focus at work. Six months later, she was taken to the Emergency Department with a severe headache and blood pressure reading of 210/100.
2. SB, a toddler age two years, was diagnosed with an ear infection. Her mother was told to give her a teaspoon of an antibiotic twice daily. So, twice a day, the mother poured a teaspoon of the medicine into her daughter’s ears.
3. A man, age 62 years, stopped taking his atenolol because he did not like how it made him feel. Thirty-five days later, he was readmitted to the hospital with a second heart attack.
4. A man, age 37 years, got a prescription for nicotine patches to help him quit smoking. He plastered the nicotine patch on his mouth.
5. A woman, age 25 years, with depression stopped taking her Prozac because she did not feel better after two weeks. Her clinician did not tell her that it may take four to six weeks to feel the full effects of the medication.

Reasons for Misuse
These are only a few examples of the thousands of people who fail to achieve the desired therapeutic outcomes from their medications because they are not taking them appropriately. Reasons include a lack of knowledge about the medication; side effects or adverse events; forgetfulness; lack of social support; cultural, health and/or religious beliefs; denial of conditions; financial challenges; poor relationships with clinicians; and lack of health literacy.

Chronic Conditions
In patients with chronic conditions who must take medications for long periods of time, misuse is especially prominent—37%-80% vary from prescription—resulting in an increase of the following: risk of mortality and morbidity; hospitalizations and length of stay, especially in patients with multiple disease states; progression of disease in patients with chronic conditions; resistance to medications; and a loss of productivity at school and work.

In 2001, one in two prescriptions dispensed, or 1.5 billion prescriptions, were not taken as directed.

Cost of Adverse Events
According to the Centers for Disease Control and Prevention and the Care Management Society of America, medication-use challenges and adverse medication events are the fourth leading cause of death in the US—after heart disease, cancer, and stroke; they are also the leading cause of accidental death in the US—ranking above motor vehicle accidents. Economically, medication-use challenges and poor adherence to cardiovascular treatments costs the US health care system an estimated $100 billion annually. Nearly 10% of hospital admissions have been attributed to medication-use challenges, of which 2%-5% were preventable. An estimated one in five elderly patients (23%) who enter nursing homes are there because they cannot or will not manage their medication appropriately.

Adverse Outcomes
Clinically, variations of medication use from prescription adversely affect patient outcomes; for example,
heart failure patients who don’t take their medications as prescribed have a two-fold increase in adverse outcomes. Beta-blocker nonadherence in patients with coronary artery disease increases mortality 4.5 times. Medication use challenges increase hospitalizations and length of stay for patients with multiple disease states and can cause disease progression. For example, hypertension can progress to an acute myocardial infarction. Medication use challenges significantly affects our health care systems and our economy. Conversely, the Heart Outcomes Prevention Evaluation study, the Scandinavian Simvastatin Survival Study Group research, and other studies have demonstrated significant improvement in mortality, by up to 40%, when medications are used appropriately.

### The B-SMART Appropriate Medication Use Process

We present here, in two parts, the B-SMART (Barriers, Solutions, Motivation, Adherence Tools, Relationships, and Triage) Appropriate Medication Use Process, a multifaceted approach that combines many of the elements listed in Table 1.

Table 1. Elements of multifaceted approaches

| Positive relationships and quality of the clinical environment | Ongoing reinforcement, motivation, and support at every step in the health care system |
| Simplifying dosage regimens | Involving patients in the decision-making process and setting goals that are later reviewed with the patient |
| Education about the medication, its benefits, side-effect management, duration of therapy, and what a patient can expect | Follow-up care and reminders |
| Rewards for achieving goals | Social support, including family members when possible |
| Self-management training |

### Barriers: Identify barriers and assess readiness to change

How to Identify Barriers—Identifying the barriers to a patient’s appropriate medication use is the first step to determining what interventions a clinician may use for that particular patient. Key barriers may be patient related, medication related, or clinician related (Table 2). A good rapport between the patient and the clinician is critical to adherence. Patients must feel comfortable about asking prescription-related questions, otherwise they will not ask.

Clinicians must first understand why a patient is not taking his or her medications properly. Some questions to better understand the patient include (depending on the situation):  

1. During the last week, how many days have you missed taking any of your medications?  
2. During the last week, what percentage of your medications have you taken?

### Table 2. Barriers to appropriate medication use and adherence

<table>
<thead>
<tr>
<th>Patient-related barriers</th>
<th>Medication-related barriers</th>
<th>Clinician-related barriers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forgetfulness</td>
<td>Complex medication regimens</td>
<td>Poor relationship with clinician</td>
</tr>
<tr>
<td>Lack of knowledge about medication and its use</td>
<td>Side effects or adverse effects from the medication</td>
<td>Poor communication with clinician</td>
</tr>
<tr>
<td>Cultural, health, and/or religious beliefs about the medication</td>
<td>Taking multiple medications at the same time</td>
<td>Cultural, health, and/or religious beliefs—disparity between clinician and patient</td>
</tr>
<tr>
<td>Denial or ambivalence regarding conditions</td>
<td>Length of therapy</td>
<td>Lack of feedback and ongoing reinforcement from clinician</td>
</tr>
<tr>
<td>Financial challenges</td>
<td>Lack of health literacy</td>
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<tr>
<td>Lack of social support</td>
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This process creates a consistent method to help patients more effectively use their medications.

Part one will address the barriers, solutions, and motivations in appropriate medication use. Part two, which will appear in the Spring 2009 issue of *The Permanente Journal*, will discuss adherence tools, relationships, and triage.

### Barriers: Identify barriers and assess readiness to change

How to Identify Barriers—Identifying the barriers to a patient’s appropriate medication use is the first step to determining what interventions a clinician may use for that particular patient. Key barriers may be patient related, medication related, or clinician related (Table 2). A good rapport between the patient and the clinician is critical to adherence. Patients must feel comfortable about asking prescription-related questions, otherwise they will not ask.

Clinicians must first understand why a patient is not taking his or her medications properly. Some questions to better understand the patient include (depending on the situation):

1. During the last week, how many days have you missed taking any of your medications?  
2. During the last week, what percentage of your medications have you taken?
3. Have you stopped or started taking any of your medications on your own?
4. Have you ever had difficulty taking your medications as prescribed and, if so, why?
5. What gets in the way of taking your medications on some days?
6. What did your doctor tell you this medication is for? (to identify patient’s knowledge and purpose of medication)
7. Have you experienced any problems or had any side effects while taking your medications?

Another question set used to screen for appropriate medication use is the Morisky Medication Adherence Scale:16

1. Do you ever forget to take your medications?
2. Are you careless at times about taking your medications?
3. When you feel better, do you sometimes stop taking your medications?
4. Sometimes, if you feel worse when you take your medications, do you stop taking them?

This question set is rated on a yes-no basis: high adherence = all “no” responses; medium adherence = 1 or 2 “yes” responses; low adherence = 3 or 4 “yes” responses.

When screening for appropriate medication use, communicate in an empathic, nonjudgmental, collaborative way and ask open-ended questions. This will improve the chance of the patient talking about his/her barriers to medication use as prescribed. Patient responses can guide areas to be addressed and allow collaborative solutions with the patient.

**Exploring Readiness to Change**—To ensure optimal outcomes, it’s critical to assess whether a patient is ready to accept a condition and/or use the prescribed medications as a component of his/her overall health care plan. Assessment is especially necessary in patients who will be taking medications for an extended period of time (for example, antihypertensive medications). The clinician must elicit any and all perceived obstacles to medication adherence. The use of the word “but” is an alert of significant ambivalence. Tools and skills to assess readiness and to motivate patients to optimize their medication use include The Readiness Assessment Ruler (Figure 1).17 The readiness ruler with a scale from 0–10 is an efficient tool for measuring how a patient feels about taking a medication for a long period of time. Exploring readiness helps the patient uncover and build his/her motivation to change habits and to accept a new therapy; it guides the clinician to effectively tailor the intervention to support movement toward change. Follow-up questions to elicit patient perspective and engage them in planning goals and problem solving include:

1. What is your understanding of the disease or condition you have?
2. What are your personal reasons for wanting to get better, reaching a specific goal concerning your condition, and/or controlling your disease or condition?
3. How can I help you?

Using a nonjudgmental and positive tone will help a patient open up. Avoid the word “why” because it has a judgmental connotation.

**Readiness stages**—There are three readiness stages: not ready, not sure, and ready to take action (Figure 1):

**Not ready (readiness ruler: 0–3):** The patient is not even thinking about the need to change. He may respond to these questions by saying, “I don’t really have a problem,” or “the doctor fixed it already.” At this point, it may be best to help the patient become more aware of his or her condition and link disease and consequences, as well as the benefits of early treatment.

**Not sure (readiness ruler: 4–6):** The patient is considering change but is ambivalent and has not yet taken any action. His responses to these questions may include, “I know I need to take my medication(s) but I don’t have the time to change.” For these patients, it’s best to reinforce their understanding of the need to change while teaching them skills and providing the necessary tools. This is the “yes, but” stage in the change process.

**Ready to take action (readiness ruler: 7–10):** The patient is ready to make the necessary changes to improve his or her health. These patients need help with goal setting, medication plans, progress diaries, as well as support when pitfalls occur. Reenforcing goals at each visit and providing positive feedback will help improve outcomes. The more positive and encouraging the
clinician, the better the outcome. Ideally, these patients need ongoing motivation, recognition, and rewards. Recognition and rewards can be congratulatory praise, an encouraging word, or even a handwritten note. “Cheerleading” from the clinician at each encounter will help sustain success.

**Solutions: Provide solutions to nine challenges**  
Once we have screened for barriers and assessed for readiness, the next step is tailoring the interventions to the identified barrier(s). The consultation should include collaborative solutions, involving patient and clinician, as well as professional advice given in a manner that enhances patient motivation. Discussed below are examples of nine challenges and their corresponding collaborative solutions to optimize the patient’s therapeutic outcomes. Although some barriers are more difficult to detect and assess, successfully identifying them can make a significant difference in patients reaching their goals.

**Challenge 1: Forgetfulness: “I forgot to take my medication”—**  
One of the most common reasons for patients not taking their medications appropriately is simple forgetfulness. In a survey conducted in the US in 2005, nearly two-thirds (64%) of patients who were prescribed regular medication reported that they had simply forgotten to take their medication, with 11% saying that this has happened “often” or “very often.” Patients with chronic conditions are more likely to forget, primarily because of the duration of time they have to take the medication (sometimes lifelong), as well as work or school schedules and other activities.

**Solution**—There are many adherence and memory tools to help patients overcome forgetfulness, which includes remembering to take medications, remembering if they have taken them, and remembering to refill prescriptions. Some collaborative solutions to forgetfulness are:

- Pill organizers and reminders, including electronic devices
- Linking medication regimen to daily habits
- Pharmacy-generated written prescription information
- Visual aids
- Follow-up management in one to two weeks.

**Challenge 2: Lack of knowledge: “I don’t know why I have to take this medication” or “I’m not sure it will do me any good”—** Helping patients understand the purpose and benefits of their medications can improve their adherence.

**Solution**—A study concluded there was an association between the occurrence of certain adverse drug outcomes and a patient’s lack of knowledge and poor perceptions about drugs. Providing this information in terms of benefit to the patient (value-added knowledge) is a powerful way of improving patients’ ability to use their medications. A survey of over 1000 adults, who admitted that they did not always take their medications as directed, revealed that 70% of the respondents said that they would be more adherent to their medication regimen if they were better informed about their disease or condition and what the prescribed medication was supposed to do. Studies show that a patient knowing the purpose of a medication, how to take a medication, and the duration of therapy, whenever possible, is vital to helping that patient obtain the optimal outcome from a medication. Some collaborative solutions to lack of knowledge are:

- Pharmaceutical pearls to help patient understand the benefits of the medication
- Pharmacy-generated written prescription information
- Visual aids
- Teach-back method
- Follow-up management in one to two weeks.

**Challenge 3: Side effects or adverse events: “I had a stomach ache when I took the medication” or “I could not do my job when I was taking this medication because of the side effects”—** Of patients on medications, 20–60% stop taking their medications as prescribed because of side-effect issues. In patients on tricyclic antidepressants, up to 50% stop taking their medications because of the adverse effects.

**Solution**—Clinicians should proactively inform patients about common side effects, what they can do to minimize them, and how long the side effects may last. Patients will be empowered by knowing what to expect and what to do when they experience the side effect. Ultimately, this solution will improve their adherence to their medication regimen. Some collaborative solutions to management of side effects are:

- Pharmaceutical pearls about side effects
- Pharmacist-generated written prescription information
- Follow-up management in one to two weeks.

**Challenge 4: Complex medication regimens: “I am taking too many medications and I cannot remember how to take them”—** In a Kaiser Family Foundation and Commonwealth Fund survey, 46% of nearly 18,000 seniors took five or more prescriptions daily. … and 4 in 10 seniors do not take medications as prescribed …
of nearly 18,000 seniors took five or more prescriptions daily. Patients with multiple chronic conditions can take up to ten different medications daily. It is no wonder a significant number are confused about taking them properly. The number of times the medication is taken daily can compound nonadherence. According to one study, there is a direct correlation between the dosing frequency and level of adherence—as dosing frequencies increase, adherence decreases steadily.

Solution—When designing medication regimens, consider frequency, dosage, and the patient’s lifestyle; eg, if the patient works at night and sleeps during the day, medications that generally make a patient drowsy and are recommended for evening use may need to be switched to daytime. Some collaborative solutions to management of complex medication regimens are:

- Adherence tools; eg, pill boxes and reminder calls
- Combination medications to simplify regimens, for example, Metaglip [glipizide (Glucotrol) and metformin (Glucophage)]
- Frequency of dose modification
- Help patients make associations, linking medication use with daily habits
- Follow-up management in one to two weeks.

Challenge 5: Denial of conditions: “I am not really sick” or “I do not need this medication”—Patients who have been newly diagnosed with a chronic condition may be in denial or have significant ambivalence about taking medications; as many as 50% of all prescriptions written at Kaiser Permanente go unfilled. Also, patients who have been on long-term medications for chronic conditions and are not experiencing symptoms sometimes feel that they no longer need to take their medications. Motivational Interviewing for health behavior change tools are most helpful.

Solution—Assessing whether or not newly diagnosed patients are ready to accept their condition and/or use the prescribed medications as a component of their overall health care plan is an important step in ensuring optimal outcomes. Some collaborative solutions for addressing denial of conditions are:

- Explore readiness to accept the disease condition
- Educate about the disease condition
- Provide pharmaceutical pearls to help patient understand the benefits of the medication
- Follow-up management in one to two weeks.

Challenge 6: Cultural or religious biases: “I do not believe in taking this medication” or “I do not need this medication”—In some cultures, diseases are looked upon as “punishment by God” for breaking religious tradition, or as a curse from another person or supernatural entity. In these cases, a person believes that taking western medication may not work to control or heal the disease. Also, a medication’s name, such as “human insulin,” may be misunderstood by the patient as signifying manufacture from human flesh or pancreas, leading to noncompliance. Each person comes to the encounter with a highly personal belief set about care and medications.

Solution—If clinicians have long-term relationships with their patients, they may wish to be acquainted with their patients’ religious and cultural practices. This may help them anticipate and develop insight into potential conflicts between adherence to treatment and adherence to theological obligations. Some collaborative solutions for addressing cultural or religious biases are:

- Using the LEARN framework to explore and understand patients’ beliefs (see Sidebar: LEARN Framework)
- Provide pharmaceutical pearls to understand the benefits of the medication
- Follow-up management in one to two weeks.

Challenge 7: Lack of financial support: “This medicine is too expensive” or “I cannot afford this medication”—Research has shown that cost of medications is associated with medication adher-

**LEARN Framework**

- **L** – Listen with empathy and understanding to the patients’ beliefs.
- **E** – Explore and understand the patient’s beliefs (utilize an interpreter when needed) and explain your perceptions of the problem.
- **A** – Acknowledge and discuss the similarities and differences between the clinician and patient’s beliefs. Be respectful of the patient’s beliefs; do not discount what the patient is saying, especially if s/he believes it’s working.
- **R** – Recommend treatment. On the basis of these insights, develop a medication plan that will minimize these conflicts. Whenever possible, offer patients the counsel and information necessary to maintain both their faith and their health.
- **N** – Negotiate an agreement. When appropriate, include family members in mediation discussions and stress the importance of family support in long-term chronic conditions.
ence. In a national survey of 875 adults with diabetes treated with hypoglycemic medication, 11% reported taking less medication because of cost. In addition, patients who have transportation issues or cannot financially take time off from work to pick up prescriptions may not adhere to their medication regimen.

**Solution**—Inquiring about patients’ copay amounts and/or their ability to pay for medications is important to helping their adherence. Some collaborative solutions for addressing financial limitations are:

- Prescribing generic drugs rather than brand names
- Mail-order drug discount programs
- Medical financial assistance
- Pharmaceutical company programs

**Challenge 8: Depression**—Depressive symptoms have been significantly associated with medication nonadherence. Depressed patients are more than twice as likely not to take their medications as prescribed, which prevents them from receiving the medication’s benefits. Other studies have shown that patients who are depressed have a 70% increased rate of CHD events, including nonfatal myocardial infarction and CHD death, compared with those who are not depressed.

**Solution**—Identify and address underlying depressive symptoms by using assessment tools: Center for Epidemiologic Studies Depression (CES-D) Scale Mood Evaluation, the Geriatric Depression Scale (GDS), the Patient Health Questionnaire (PHQ9, PHQ2), and the Beck Depression Inventory for Primary Care (BDI-PC).

- Identify depressive symptoms
- Use available tools to assess effectiveness of psychological and/or medication treatments
- Follow-up management in one to two weeks.

**Challenge 9: Poor health literacy**—Health literacy is a constellation of skills that constitutes the ability to perform basic reading and numerical tasks for functioning in the health care environment and acting on health care information. Low health literacy is common in the US, affecting nearly 90 million adult Americans. Low health literacy results in difficulty understanding and acting upon health information, and, according to the Institute of Medicine report, costs the American health care system about $58 billion per year. This can adversely affect the clinician-patient relationship, leading to substandard medical care and poor understanding of written or spoken medical advice, adverse health outcomes, and a negative effect on the health of the population.

A study of Medicare enrollees in a national managed care organization showed that 54.3% of enrollees with inadequate literacy levels did not know how to take medications on an empty stomach. In a study of 114 patients with diabetes, researchers found only half of those with inadequate health literacy knew the symptoms of hypoglycemia, or low blood sugar. Research also suggests that people with low health literacy make more medication or treatment errors and are less likely to comply with recommended treatment. In fact, an American Medical Association committee report showed that health literacy correlates more strongly with overall health status than education level or any other sociodemographic variables, including income. Additional health literacy information can be found at: [http://ambulatorypractice.org/dls/Health_Literacy/start.htm](http://ambulatorypractice.org/dls/Health_Literacy/start.htm).

**Solution**—Improve patients’ health literacy by helping them to understand how to use their medications and how their medications work.

- Provide pharmaceutical pearls to help patient understand the benefits of the medication
- Provide interpreter services for patients who do not speak English
- Provide patient medication information at the fourth-grade level
- Use nonmedical language and speak slowly
- Provide information in an organized manner
- Use visual aids whenever possible
- Use the “teach-back method” to check for comprehension.

**Motivation: Helping patients help themselves**

To motivate people to change, we must first help them recognize their personal benefits to making a health-activity change. This can be done by linking the problem to things they care about, while maintaining a warm, nonjudgmental style of interaction. For example, when exploring readiness to change, a clinician may discover that the patient hopes to live long enough to see the birth of his or her grandchildren. This deep personal desire can encourage patients to take medications consistently, to change their diet, and to exercise. It can also be linked to specific health goals, for example, in a diabetic patient—getting HgA1c under 7. Whatever health goal is set, the patient is more likely to follow through on the necessary health behaviors that will make that goal a reality if it’s linked to strong personal motivators.

**Goal setting**—People who write out their goals and have an action plan are as much as ten times more likely to achieve their goals than those who only think about them. To help patients appropriately use
their medications, clinicians should set clear health goals in a collaborative manner and encourage patients to write these down. Each time the patient has contact with a clinician on his or her health care team, that clinician should review these health goals and provide feedback.

Set goals in stages so patients can celebrate every small step that is achieved toward their larger goal. For obese patients, this could be setting a small goal of losing 10% of their body mass. For patients who are physically inactive, an initial goal could be to walk a short distance every day for a week, building up to a mile or more. For a diabetic who forgets to test blood sugar, the initial goal may merely be daily glucose testing; once this is achieved, and is sustained for some time, the patient can move on to other diet and lifestyle changes to support a healthy blood sugar range.

The Three Es: Educating, empowering, and encouraging—Educating patients about their disease conditions and medication treatment plans is essential if patients are to successfully use their medications appropriately to achieve the optimal therapeutic outcomes. Educating patients includes providing concise and focused verbal information about their condition and medication treatment plan and providing written information to reinforce what’s been discussed, whenever possible. Behavioral tools, such as follow-up phone calls and reminder postcards, must be used to help patients take their medications as prescribed. Educating patients will empower them to take control of their own health issues. Last but not least, encouragement and support from clinicians and family members will help patients exert greater effort. Clinicians can create a positive interaction that motivates patients to excel by encouraging goal sharing, setting clear objectives, discussing goals at each visit, and providing positive feedback. The value of a clinician recognizing and acknowledging patients when both small goals, or large milestones, are accomplished cannot be overstated.

Summary
Research shows that the combination of education, empowerment of patients by providing tools and feedback, and ongoing encouragement given to patients will significantly improve adherence to therapy plans and improve outcomes than any one component alone.21,24

To complete this B-SMART approach to medication optimization, part 2 of this article in the Spring 2009 issue will discuss: Adherence Tools: Tools and reminders to keep patients on track; Relationships: Building positive relationships; and Triage: Direct patients’ medication management plan into the broader health care system.

Disclosure Statement
The author(s) have no conflicts of interest to disclose.

References
How Things Have Changed

“Six of the patients have died, sir,” said the hospital nurse to the physician, as he went on his rounds. “Why, I wrote the medicine for seven,” mused the doctor, passing to another ward. “Yes, but one of them wouldn’t take his,” was the naïve reply.

—Anonymous, circa 1850
Image Diagnosis: Foot Fractures

Gus M Garmel, MD, FACEP, FAAEM

Figure 1. (above, left) Anteroposterior (AP) view of the foot and Figure 2. (above, right) Oblique radiograph of the same foot.

Two views of an injured foot demonstrates disruption of the Lisfranc joint consistent with a Lisfranc fracture-dislocation. Although it is difficult to see a fracture fragment in these films, significant force is needed to disrupt this strong joint which stabilizes the midfoot, often resulting in a fracture at the base of the 2nd metatarsal or one of the cuneiforms. If the diagnosis is in question, a weight-bearing anteroposterior view or a computed tomography scan of the foot may identify this injury. Surgical repair is generally necessary. Compartment syndrome of the foot is a possible complication.

Figure 3. (left) Lisfranc joint illustration. Used with permission, Sonia Y Johnson, MD.

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Figure 4. (left) Arrows identify a fracture through the calcaneus.

Angle formed by the intersection of the line connecting the tuberosity and the highest point of the posterior facet with the line connecting the posterior facet and the posterior process of the calcaneus determine Bohler’s angle. This angle is normally 20-40 degrees, but can be reduced in some fractures of the calcaneus. In this image, Bohler’s angle measures just less than 20 degrees, as this fracture is only minimally displaced.

**Clinical Pearl:** Calcaneus fractures can be associated with vertebral body fractures of the spine. They carry the eponym “lover’s fracture” due to jumping from a height (such as a balcony or second-floor window).

Figure 5. (right) Arrow points to a horizontal fracture line as well as surrounding soft tissue swelling. As this fracture is due to an acute injury, the area of swelling is likely to be tender to palpation.

Jones fracture is due to an acute injury to the lateral midfoot. The fracture line should be located within 1.5 cm distal to the tuberosity of the 5th metatarsal in a horizontal plane. This fracture should not be confused with the more common avulsion fracture at the base of the 5th metatarsal styloid, as treatment differs.
Stuart Hahn, MD, is a Family Practice Physician and Clinical Director of the Sacramento Appointment and Advice Call Center. This photograph was taken in Homer, Alaska, with a hand held Canon 1D Mark II N at 500 mm, 1/1000 sec at F10, ISO 400. Dr Hahn adjusted the image in Photoshop for contrast, sharpness, and saturation.

"Eagle"

Photograph

By Stuart Hahn, MD
Corridor Consult

Evaluation of Hypertension with Hypokalemia

Antoine C Abcar, MD
Dean A Kujubu, MD

Vignette

Your colleague asks for your suggestions on the evaluation and treatment of a woman age 70 years with a five-year history of hypertension who has required progressively more medication because of persistent high blood pressure. She is taking five medications, including a diuretic, but still has a blood pressure of 165/95 mm Hg (well above the current standard definition of hypertension of 140/90 mm Hg). He says that the patient is asymptomatic and that her physical examination was normal. The patient’s serum potassium levels have ranged from 3.2 to 3.5 mEq/L for many years despite potassium supplementation, which had been attributed to her diuretic use. Her renal function is normal.

Discussion

Common Causes of Poorly Controlled Hypertension

Hypertension that remains in poor control despite the use of many medications is a difficult problem that every primary care physician has faced. Common causes of uncontrolled hypertension include white coat hypertension, nonadherence to a salt-restricted diet or to a medication regimen, failure to include a diuretic in the antihypertensive regimen, use of concurrent medications such as nonsteroidal anti-inflammatory agents or oral contraceptives, obesity, obstructive sleep apnea, and parenchymal renal disease. Home blood pressure measurements or 24-hour ambulatory blood pressure monitoring are useful in the evaluation for white coat hypertension. Obtaining a 24-hour urine collection for sodium and creatinine to assess dietary sodium intake is frequently helpful. An otherwise healthy patient ingesting a diet limited to 2000 mg of sodium should excrete no more than 87 mEq of sodium in a 24-hour urine sample; higher amounts of sodium excretion suggest dietary nonadherence. Symptoms such as daytime somnolence, not feeling rested after a full night of sleep, mood disturbances, and a lack of concentration suggest that obstructive sleep apnea should be considered and a sleep study ordered. A frank discussion with the patient about the importance of blood pressure control on cardiovascular health, the adherence to medication regimens despite potential side effects, and the benefits of exercise, weight loss, smoking cessation, and reduction of alcohol intake are essential.

Any efforts to simplify the medical regimen will help with patient adherence.

Less Common Causes of Poorly Controlled Hypertension

Although the majority of hypertension in the adult population is essential hypertension, in selected cases it is reasonable to evaluate for possible secondary causes of hypertension. Hypertension of new onset in patients younger than age 30 years or of sudden onset in those older than age 50 years; hypertension in the absence of obesity; the lack of a strong family history of hypertension; the requirement for three or more medications, one of which is a diuretic, with suboptimal control; the acute deterioration of renal function with the initiation of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-receptor blockers (ARBs); paroxysmal symptoms of anxiety, diaphoresis, or palpitations; Cushingoid features; renal dysfunction; and the presence of hypokalemia and metabolic alkalosis are all findings suggestive of secondary hypertension. Because this patient has a relatively late onset of worsening hypertension, persistent hypokalemia despite potassium supplementation, and resistant hypertension, it is reasonable to evaluate her for underlying causes of hypertension.

The most common cause of hypokalemia in a hypertensive patient is diuretic use. By enhancing urinary flow and sodium delivery through the collecting tubule, both thiazide and loop diuretics promote renal potassium secretion. Potassium secretion is further enhanced in the setting of diuretic-induced...
The majority of hypertension in the adult population is essential hypertension... the benefits of exercise, weight loss, smoking cessation, and reduction of alcohol intake are essential.

intravascular volume depletion and secondary aldosterone stimulation. Hypokalemia may also result from gastrointestinal problems, such as diarrhea or vomiting, though these patients would generally not be hypertensive. Magnesium deficiency due to malabsorption, poor dietary intake, or exposure to medications such as aminoglycosides is another cause of persistent hypokalemia. Spontaneous hypokalemia, in the absence of diuretic use, deserves further evaluation.

The most common causes of hypertension with hypokalemia are presented in Table 1. Primary aldosteronism, or Conn’s syndrome, previously thought to be an uncommon condition, in some studies is now seen to account for between 5% and 13% of all hypertension; the increase in diagnoses is due to the advent of more widespread screening. Although hypokalemia and metabolic alkalosis are classic findings of primary aldosteronism, hypokalemia is seen in only 20% to 50% of documented cases. The ratio of plasma aldosterone concentration to plasma renin activity (PAC:PRA) is widely used as a first step in evaluating patients with both hypertension and hypokalemia. If the morning PAC:PRA is >30, with PRA expressed as ng/mL per hour, and the PAC is >15 ng/dL, the results are highly suggestive of primary aldosteronism. Relying solely on an elevated PAC:PRA without attention to the level of PAC may yield false positive results because patients with low-renin essential hypertension will be included. Aside from stopping aldosterone-receptor antagonists, such as spironolactone or eplerenone, for six weeks, there is no need initially to stop other antihypertensive medications before obtaining a PAC:PRA. Of course, a more representative PAC:PRA is obtained if other antihypertensive medications that may affect the ratio are likewise withheld; however, this is rarely practical. Diuretics, ACEIs, and ARBs increase renin levels, which may lead to a low PAC:PRA; in contrast, β-blockers and clonidine reduce renin secretion, resulting in a higher PAC:PRA than would be seen in their absence. Since hypokalemia itself inhibits aldosterone secretion, potassium depletion should be corrected before the PAC:PRA is obtained. PAC and PRA values are highly laboratory dependent, and the calculated ratio depends on the units used to express concentration or activity. Moreover, since aldosterone is secreted in bursts, the PAC:PRA could change within minutes. Early morning levels are most representative. The decision about whom to evaluate further for primary aldosteronism should not be dependent on only one determination of PAC:PRA. If repeated determinations demonstrate a PAC:PRA >30 and a PAC >15 ng/dL, confirmatory biochemical testing, such as measuring PAC before and after 2 L of normal saline administration or a 24-hour urinary aldosterone excretion after three days of oral salt loading (six g sodium chloride) with careful blood pressure monitoring is indicated to diagnose primary aldosteronism. Neither oral salt loading nor saline infusion should suppress the autonomously secreted hormone from an adenoma. The clinical response to a trial of aldosterone-receptor antagonists is not in itself diagnostic of primary aldosteronism, because many patients with resistant essential hypertension have a favorable response to these medications. Consultation with a nephrologist or endocrinologist may be helpful for advice on conducting these tests correctly.

Another cause of hypertension with hypokalemia is Cushing’s syndrome. Cushing’s syndrome, a result of excess endogenous glucocorticoid secretion, presents with hypertension, central obesity, abdominal striae, glucose intolerance, depression, weakness, and characteristic moon facies. Hypokalemia is most noted in the ectopic adrenocorticotropic hormone syndrome. It is thought that high levels of endogenously produced cortisol, corticosterone, and deoxycorticosterone stimulate the mineralocorticoid receptor, resulting in hypertension and hypokalemia. The use of aldosterone-receptor antagonists does not completely ameliorate the hypertension, suggesting that other reasons exist for hypertension in Cushing’s syndrome, aside from excessive mineralocorticoid effect. The initial screening involves collecting a 24-hour urine for free cortisol. Values that are more than three to four times normal are diagnostic for Cushing’s syndrome. Owing to the difficulty in correctly collecting a 24-hour urine sample, however, some physicians prefer performing a low-

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dexamethasone-suppression test by obtaining an 8 AM cortisol level after the administration of 1 mg of dexamethasone at bedtime (11–12 pm). A level of <5 μg/dL indicates appropriate suppression. Morning cortisol levels >5 μg/dL after low-dose dexamethasone suppression warrant further evaluation. Endocrinology consultation would be helpful.

Pheochromocytoma is classically described as presenting with paroxysms of adrenergic symptoms, such as palpitations, headaches, anxiety, and sweating, associated with labile hypertension. The clinical manifestations of a pheochromocytoma depend on the predominant catecholamine that the tumor produces and whether the secretory pattern is continuous or paroxysmal. Although pheochromocytomas are rare, autopsy studies suggest that they are present more often than they are diagnosed. These patients tend to have a decreased intravascular volume status, and thus both PRA and PAC levels are elevated. The preferred test for diagnosing pheochromocytoma is under debate. Twenty-four-hour urinary fractionated metanephrines and catecholamines may be the preferred diagnostic test, but some advocate the use of plasma-fractionated free metanephrine because of its ease of collection and high sensitivity. Negative findings on a plasma test essentially rule out pheochromocytoma as a diagnostic possibility. Medications such as levodopa, tricyclic antidepressants, buspirone, adrenergic decongestants, and amphetamines may interfere with the analytic assay. Ideally, these medications should be tapered and stopped two weeks before testing, if possible.

Renovascular hypertension, though relatively uncommon in the general hypertensive population, is increased in prevalence in both the younger (<30 years of age) and in the older (>50 years of age) patient with new-onset hypertension. Fibromuscular dysplasia is the most common cause of renovascular hypertension in the younger patient, whereas atherosclerotic vascular disease is the most common in the older patient. Both may manifest as resistant hypertension. Acute renal deterioration after administration of ACEI or ARB and recurrent episodes of flash pulmonary edema suggest either bilateral renal vascular disease or disease in a patient with a solitary kidney. The presence of a systolic–diastolic abdominal or flank bruit or a renal sonogram demonstrating marked differences in kidney sizes suggest renal vascular disease. Although renal arteriography remains the diagnostic gold standard for renovascular disease, magnetic resonance angiography techniques and computed tomography (CT) angiography have shown promise in visualizing the renal arteries without arterial cannulation. The use of gadolinium and iodinated contrast agents, however, is not without risk in patients with chronic renal impairment. Both gadolinium and iodinated contrast agents have nephrotoxic potential. Moreover, gadolinium use in patients with an estimated glomerular filtration rate of <30 mL/min has on rare occasions been associated with nephrogenic fibrosing dermopathy, a progressive sclerodermatous condition for which there is no defined treatment. For this reason, nonenhanced magnetic resonance imaging (MRI) or carbon dioxide angiography to avoid the use of iodinated contrast agents has been tried with some success. Duplex ultrasonography has been used in some institutions in selected patients to visualize the renal arteries and measure hemodynamic changes within them. The latter is technically demanding, and its success depends on the skill of the operator and on the patient’s body habitus. Captopril-enhanced nuclear medicine renal scanning, which images the differential perfusion of the kidneys, may fail to detect bilateral renal artery disease. If findings suggestive of hemodynamically important stenosis are discovered, renal arteriography may be indicated, particularly if the patient is a candidate for either surgical revascularization, angioplasty, stent deployment, or all of these procedures. Whereas revascularization is often successful in alleviating hypertension in patients with fibromuscular dysplasia, the long-term results with atherosclerotic renal artery disease are less promising. The optimal treatment for atherosclerotic renal vascular disease remains primarily medical.

Finally, hypertension from any cause, if unmanaged, may enter into an accelerated phase, resulting in a hypertensive emergency. Manifestations include encephalopathy, retinopathy, pulmonary edema, acute renal failure, and microangiopathic hemolytic anemia. Hypertensive crisis is a state of intense vasoconstriction; PRA and PAC levels are generally markedly elevated. Catecholamine levels may also be elevated. Hypokalemia is frequently found on presentation. Evaluation for secondary causes of hypertension should be postponed until after hypertension is better controlled and the vasoconstricted state is corrected.

**Conclusion**

The patient whose case is described here deserves evaluation...
for an underlying cause of her resistant hypertension. An initial approach would include correction of hypokalemia with potassium supplementation, and then obtaining a random PAC:PRA, assuming that she is not taking an aldosterone-receptor antagonist. A ratio of >30, with a PAC of >15 ng/dL on repeated determinations, is highly suggestive of primary aldosteronism. Biochemical confirmation would then be indicated. If the PAC:PRA is not elevated and plasma renin activity is high, evaluation for renal vascular disease with MRI or CT angiography is reasonable because her renal function is not compromised. A 24-hour urinary fractionated metanephrines or plasma fractionated free metanephrines and a 24-hour urinary free cortisol or an overnight low-dose dexamethasone-suppression test, screening tests for pheochromocytoma and Cushing’s syndrome, respectively, may also be performed if there is clinical suspicion for these conditions. Obtaining a nephrology or endocrinology consultation to assist with the evaluation and interpretation of results should be considered.

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References

The Ischemic Kidney
These experiments indicate that, in dogs at least, ischemia localized to the kidneys is a sufficient condition for the production of persistently elevated systolic pressure. When the constriction of both main renal arteries is made only modestly severe … the elevation of systolic blood pressure is unaccompanied by signs of materially decreased renal function … . Almost complete constriction of both main renal arteries … results in great elevation of systolic blood pressure, which is accompanied by … uremia.

“Household Saints of Dubious Virtue”  
Mixed Media and Polymer Clay Sculptures  
By Marsha Balian, NP

Ms Balian is a Nurse Practitioner in the Ob/Gyn Department at the Oakland Medical Center in California. Her artwork can also be seen on the cover and page 29 and on her Web site: www.marshabalian.com.
SCPMG University: Helping New Physicians Adapt and Succeed

Jeffrey Weisz, MD
Nancy H Spiegel, MS

In July 2007, the Southern California Permanente Medical Group (SCPMG) launched SCPMG University, a program designed to help newly hired physicians adapt to their positions more quickly and lay the foundation for a successful career within the medical group.

An individual's first few months with an organization are crucial. During that period, professionals develop a sense of what is important, what the organization expects from them, and what they can expect in return. A study conducted by Texas Instruments showed that new employees who attend an onboarding program reach full productivity two months earlier than those who do not attend.1 Many companies have developed robust onboarding programs for new employees with an eye toward improving both productivity and employee retention.2,3

Building a Solid Foundation

SCPMG University consists of three all-day sessions at SCPMG’s regional headquarters in Pasadena, California and covers a comprehensive curriculum (Table 1).

Within three months of their hire date, incoming Associate Physicians generally attend SCPMG University, giving them an early introduction to the tools they will need to succeed in the organization. The rigor of the program contrasts sharply with the informal approach some long-time SCPMG partners may remember.

“My only orientation was coming in to meet my new chief and finding out my schedule. He gave me a few videos, sent me over to another building to watch them on my own, and told me to come back to start work the next day,” said Marc Klau, MD, Regional Director, Physician Education, Residency, and Leadership.

“It took a long time for me to really understand the organization—I don’t think I really figured out the finances or our quality improvement initiatives for five to seven years,” he said. “Now, we’re making sure our associates get all of that information right up front, in just a few days.”

Focusing on Inspiration and Engagement, Not Forms

Another unique aspect of the program is that it casts aside the traditional paper-heavy orientation, drawing instead on multimedia resources and interactive activities to create a more emotional, engaging experience. Examples include:

• powerful video materials, ranging from a documentary-style film about physicians rediscovering

Table 1. SCPMG University curriculum overview

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Jeffrey Weisz, MD, (left) is the Executive Medical Director of the Southern California Permanente Medical Group. E-mail: jeffrey.a.weisz@kp.org.

Nancy H Spiegel, MS, (right) is the Manager of Leadership and Organization Development for the Southern California Permanente Medical Group. E-mail: nancy.h.spiegel@kp.org.
meaning in medicine to some of the most popular television ads from Kaiser Permanente’s (KP’s) Thrive campaign
• a reading from an emotional thank-you letter from a patient who has been a member of KP for more than 50 years
• an exercise in which participants build a paper avatar representing who they are and then talk about it with their neighbors as a way of breaking the ice; and
• short skits by SCPMG’s dedicated acting troupe (the Care Actors), who recreate common office scenarios and encourage audience members to view the situation from the patients’ points of view.

Structured exercises also encourage interaction. Physicians are asked to work together as a group, for example, to evaluate the care needs of our patient population and make recommendations for specific quality improvement goals. Significant time is also set aside for physicians to ask questions of regional leaders and get advice from long-time partners.

“Physicians are presented with an unparalleled opportunity to ask questions and build professional relationships, instilling a sense of pride and belonging to the SCPMG family,” said Lucia Soh, Director of Physician Leadership and Performance, who manages the day-to-day operations of SCPMG University.

Even the seating is arranged with careful thought. Physicians sit with colleagues from their medical center on the first day, but join physicians from the same specialty on the remaining two days. This encourages physicians to get to know colleagues they might not have otherwise met, helping them build a broad network that they can tap into once they are back in their own practice.

Evaluating the Program’s Benefits
Because the program is only a year old, it is still too early to say how it will impact retention and productivity. A proposed three-year evaluation plan, which incorporates a multimodal methodology, will help us ascertain the immediate and long-term effect of the program on performance and business outcomes.

Survey data gathered from participants in SCPMG University’s first year show promising improvements in organizational knowledge. Mean scores improved significantly on 11 out of 14 items on pre- and postprogram surveys (Table 2).

We believe SCPMG University will prove to be a valuable resource for our medical group. In the future, we may introduce additional programs, including one to help physicians new to leadership positions become strong leaders in SCPMG. Offering opportunities such as these will help us attract and retain talented physicians, improve our performance as a medical group, and let our physicians know they are valued members of the Permanente family.

Disclosure Statement
The author(s) have no conflicts of interest to disclose.

References
Narrative-Based Medicine: Potential, Pitfalls, and Practice

Vera Kalitzkus, PhD
Peter F Matthiessen, MD, PhD

Introduction

Narratives have always been a vital part of medicine. Stories about patients, the experience of caring for them, and their recovery from illness have always been shared—among physicians as well as among patients and their relatives. With the evolution of “modern” medicine, narratives were increasingly neglected in favor of “facts and findings,” which were regarded as more scientific and objective. Now, in recent years medical narrative is changing—from the stories about patients and their illnesses, patient narratives and the unfolding and interwoven story between health care professionals and patients are both gaining momentum, leading to the creation or defining of narrative-based medicine (NBM). The term was coined deliberately to mark its distinction from evidence-based medicine (EBM); in fact, NBM was propagated to counteract the shortcomings of EBM. But what is NBM? Is it a specific therapeutic tool, a special form of physician-patient communication, a qualitative research tool, or does it simply signify a particular attitude towards patients and doctoring? It can be all of the above with different forms or genres of narrative or practical approach called for depending on the field of application.

In this article we will give a systematic overview of NBM: a short historic background; the various narrative genres; and an analysis of how the genres can be effectively applied in theory, research, and practice in the medical field, with a focus on possibilities and limitations of a narrative approach.

In medical practice, three different, though overlapping, areas can be distinguished:
1. Learning the patient’s and the caregiver’s perspective for research and training. Classification of various narrative forms or genres will be included in this discussion.
2. The narrative approach in medical practice, through understanding the narrative structure of medical knowledge, and narrative-oriented, physician-patient relations.
3. Narratives as evidence—narratives from social science research and narratives derived from medical practice and patient encounters are a source of knowledge for evidence, beyond the gold standard of randomized controlled trials of evidence-based medicine.

Background

Medical narrative is changing: a movement from the physician’s narrative to patient’s narrative. In modern times, the dominant medical narrative has been the physician’s narrative in the form of the classical objective biomedical scientific report. The medical narrative nowadays, David Morris points out, increasingly recounts the patient narrative. In the late 1980s, Polkinghorne and others spoke about a “narrative turn” in the medical field—narratives are now seen as a useful resource for understanding the individual, patient-specific meaning of an illness.

Narratives—especially patient narratives—incorporate the question of causality and thus foster an understanding of the patient’s illness perception. In the words of Greenhalgh and Hurwitz, “Narrative provides meaning, context, perspective for the patient’s predicament. It defines how, why, and what way he or she is ill. It offers, in short, a possibility of understanding which cannot be arrived at by any other means.” This understanding, we believe, is also true for stories about being a medical professional and caring for the sick in times of growing economic and institutional constraints; and with the increasing dominance of the economic narrative.

Narrative Structure of Medical Knowledge

The development of NBM has to be understood in the context of patient-centered approaches—bringing

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the patient as a subject back into medicine. This has been central to Viktor von Weizsäcker’s work on psychosomatic medicine. He demanded inclusion of the patients’ experience into the medical endeavor. An illness narrative tells us not only about a specific medical case, but about the intensive, ultimate, and most authentic reality of life or death of a person. According to von Weizsäcker, the illness narrative is not only a description of something pathological; it is the description of the life of the illness in that specific individual human being. This subjective approach can also be found in patient-oriented, physician-patient communication and relations extending back to Carl Rogers and Michael Balint. In 1998, Greenhalgh and Hurwitz pointed out that the meaning of narratives in the physician-patient interaction becomes apparent in those subjective, patient-oriented encounters, especially in Balint groups.

Kathryn Montgomery Hunter was one of the first to point out the narrative structure of medical knowledge: “Narrative is the ultimate device of casuistry in medicine (as in theology and law), which enables practitioners who share its diagnostic and therapeutic worldview to fit general principles to the single case and to achieve a degree of generalization that is both practicable and open to change.”

In that sense narratives can be understood as the bridge between the evidence of large scale randomized-controlled studies and the medical art of applying this knowledge to a single case. EBM and NBM thus must be understood in complementary terms. Peter F Matthiessen points out: In medical practice, both aspects, the search for laws of cause and effect and the description of the specific, unique and singular cannot be pursued separately; they are inextricably intertwined. In the process of turning medicine toward a natural science, the effort to reach ever more objective findings led to neglect of the subjective dimensions of medical practice. Matthiessen argues that an incorporation of the subjective areas (for example in single case studies) would result in a higher objectivity within medicine. According to Matthiessen, a narrative culture in medicine would highlight the interpretative and judgmental character of diagnostic statements. It would further clarify the intrinsic contextuality of knowledge. He concludes that objectivity in that sense would be the methodological inclusion of the subjectivity of all perception and knowledge. The latest development in the field has led to the endeavor to integrate the approaches of EBM and NBM in a program called “narrative evidence-based medicine” that, according to one of its founders Rita Charon, “recognises the narrative features of all data and the evidentiary status of all clinical text.”

The Different Genres of Narratives

Narratives about being ill and caring for the ill provide insight into respective experience and thus could foster mutual understanding—not only from the medical side for their patients but also from patients for their caregivers. Narratives also give further insight into the cultural and sociohistoric context of medicine and being ill. Four genres of narrative can be distinguished:

1. **Patient Stories—Classic Illness Narratives**

Patient stories allow making sense of their suffering and how it feels from the inside. They offer a biographic and social context of the illness experience and suggest coping strategies. They also create potential for personal development. Jeffrey K Aronson, MD, MBChB, FRCP, DPhil, Professor in the Department of Clinical Pharmacology at the University of Oxford, has created an annotated bibliography of about 270 books on pathographies and autopathographies, available at: www.clinpharm.ox.ac.uk/JKA/patientstale.

2. **Physicians’ Stories**

Autobiographical accounts about life as a physician and caring for those who are sick have a long history—one prominent example being the writings of Anton Chekhov. Physicians’ stories can also contribute to the rehumanization of medicine in the same way as patient narratives. After all, human beings deliver medical care. A special genre constitutes stories about physicians as patients. Reflections on physicians’ own vulnerability are not very prominent, and even less so in public; however, these accounts show how physicians’ illness experiences changed their understanding of their professional role and their relation to their patients. DasGupta and Charon tried to foster that kind of reflexivity—ie, taking on a reflexive stance toward their own experience—in medical students, asking them to write about a time of experienced bodily vulnerability or suffering. This means of reflection helps physicians to develop empathy and understanding for the situation of their patients. DasGupta and Charon conclude: “The personal illness narrative allows the reader-writer to more fully enter the reality of the patient world by recognizing, describing, and integrating the similari-
ties in her own personal experiences and those of the patient. It can also counteract the neglect of their embodiment that is intrinsic, unfortunately, to the medical system.

3. Narratives about Physician-Patient Encounters

Illness, and the process of being ill, is formed and articulated in the physician-patient encounter. The patients' experience of symptoms is interpreted by physicians' medical knowledge, eventually leading to a diagnosis and respective therapeutic intervention. This in turn changes patients' narratives about what they experience. As they “make sense” of their sensations, the medical perspective on them plays a vital part. There is an ongoing debate about the degree of a physician's influence in creating the patient's story and we will suggest a way to look at it in the next section of this paper. Nevertheless, physicians have the potential to take on an important supportive role in the creation of the illness narrative: to create and to formulate new stories, as family physician John Launer points out, and thus help patients in their coping process and even contributing to their personal growth. The illness narrative has to be understood and seen as being part of a patient's life story. Of course an inverse effect is possible in that patients feel devalued by medical judgment of their existence, especially if it is a strictly pathologic judgment without account of the still healthy and valuable aspects a person has even in severe illness or when the whole person story is truncated merely to the illness narrative.

4. Grand Stories—Metanarratives

In the background of individual narratives there are always grand narratives of sociocultural understandings of the body in health and illness. They are described in studies of medical history or the history of the body—such as The Culture of Pain by David B Morris or Fragments for a History of the Human Body by Michael Feher et al., and the dominant medical discourse in particular as has been analyzed by, for example, Michel Foucault. This influences both the caregivers' and the patients' view of illness and of the sick body.

The Potential of Narratives in Communication

Published narratives tend to be told in reflected and elaborated ways. But narratives are also shared in and created by communication, ie, a “speech act.” A speech act constitutes a specific form of text genre with a specific linguistic text structure that is distinct from other forms, for example an argument or a report. These nucleus narratives can also emerge in a physician-patient consultation. There are five characteristics of narratives in a speech act that are important for medical practice. These characteristics:

1. Consist of distinctive and recognizable phases: orientation, complication (an incident that is problematic or out of the ordinary; ie, the part of the story that makes it worth telling), evaluation, coda
2. Always have a specific addressee (and thus can never be told in the same way twice)
3. Always are about an individual and what s/he experiences/feels
4. Contain information that is not an essential part of the story—the content is the narrator's choice, what s/he regards as relevant to the story and thus is an act of meaning creation
5. Have the potential to “draw us in” and thus, in the words of Greenhalgh/Hurwitz enable the experience of “living through” and not only “knowledge about” (emotional). Narratives on the level of a speech act follow an intrinsic drive for completion: to give relevant context information and to bear in mind the social rules of interaction; thus reaching a conclusion of the story within a reasonable time frame. This is especially important for medical professionals who act under severe time constraints and who fear being overwhelmed by their patients' narratives, if they open that Pandora's box. This nucleus form of a narrative can emerge in a physician-patient interaction and gives the physician the specific insights as mentioned above. They can also form an element of the larger narrative evolving in the physician-patient-encounter.

Cocreation of Illness Narratives

Concerning the cocreation of the patient’s illness narrative we agree in that his/her illness narrative is formed and changed by the medical encounter (cocreation) and that this accounts for its therapeutic potential. Nevertheless, this process of cocreation in the encounter does not lead to a more or less stable narrative shared by both and recounted as such by the patient. Instead, his/her illness narrative is in the process of forming/changing through time and will be a separate form of narrative—distinct from the physician's narrative and the narrative of the encounter, although influenced by both. Likewise the physician’s story of that patient’s illness is changed by the encounter and, in consequence, can inform the
physician’s understanding of that disease—the above mentioned narrative structure of medical knowledge.\textsuperscript{1} The patient-, physician- and the encounter narrative each signify a specific type or aspect of an illness narrative, their mutual influence is always given.

Medical professionals are trained in medical history-taking with the goal of eliciting the relevant medical facts from patients without too much “useless” information. However, allowing a narrative flow in the consultation does not necessarily require a lot of time. A study about spontaneous talking time of patients in general practice points out that two minutes of listening is enough for 80\% of the patients to recount their concerns. Out of 335 patients only 7 needed more than 5 minutes. The physicians of the study were trained in \textit{active listening}, and the study cohort consisted of many \textit{difficult} patients with complex medical histories.\textsuperscript{27} “One of the most difficult tasks in health care,” John Launer states, “may be to manage each consultation so that it continually meets both narrative and normative requirements.”\textsuperscript{28} Illness narratives provide context for physiologic symptoms and results of diagnostic tests—but an illness has meaning in the biographic context of a patient. This meaning, however, must be decoded.

**The Analysis of Meaning**

Medicine has no respective theory or methods for analysis of meaning. It draws on the knowledge of interpretive sciences, such as humanities or social sciences. This is less a problem in research, where respective disciplines could be part of the research team, or for reading published accounts of illness, where the story is “processed” in order to convey its meaning to the reader. However, it becomes crucial in the context of medical practice—the actual physician-patient encounter. Rita Charon points out that literature and medicine classes for medical students and professionals can be a means to develop a respective sensitivity towards meaning-creating processes.\textsuperscript{29,30} But it might also be necessary to reflect on actual daily practice to get a feel for “narrative in action,” for example by analyzing video- or audio-recorded consultations together in a peer group. We tested that in a research project with general practitioners. In a monthly quality circle (peer review group), and additional workshops, the participants were trained in analytical methods derived from the social sciences; they then used these skills and methods to discuss recorded consultations from their own practice.\textsuperscript{30} This training helped them to identify areas of strength and weakness in their relations with patients. In addition, it had the effect of self reflection \textit{with regard to} daily practice, and \textit{during} daily practice, and helped to overcome established, hindering habits. After two years they reported a higher sensitivity for biographic context, subjective illness categories, and meaning-creating processes by the patient. It became apparent, however, that a narrative approach cannot be learned in a short course conveying a toolbox of narrative techniques. Changing from a conventional form of practice toward a narrative-oriented one asks for perseverance, vigilance against old routines and constant (self) reflection—ideally in a peer group with regular, video-documented case discussions.

Understanding the often-complicated and contradictory stories of suffering is not easy or self explaining. As Rita Charon explains: “Pain, suffering, worry, anguish, the sense of something just not being right: these are very hard to nail down in words, and so patients have very demanding ‘telling’ tasks while physicians have very demanding ‘listening’ tasks.”\textsuperscript{31} Apart from analytical skills to understand the implicit meaning in narratives, listening skills are vital for narrative practice. The necessary listening skills go beyond specific techniques. What is needed is a particular mindset of inner involvement or, as Arthur Kleinman calls it, a stance of “empathetic witnessing”\textsuperscript{32} and an all-encompassing attention: “Attention may be the most urgent goal in our work,” Rita Charon concludes, “to attend gravely, silently, absorbing oceanically that which the other says, connotes, displays, performs, and means.”\textsuperscript{31}

**The Healing Potential of Narratives**

“… [I]llness is terrible but, with some luck, it can also be full of wonders,” Arthur W Frank is convinced. “The terrors assault us at once; the wonders take longer to become visible. Stories help us gain some distance from the terrors and learn to perceive the wonders … . In telling all kinds of stories, we find healing.”\textsuperscript{33} Thus, narratives can have a healing effect—both in listening to the stories of others and in telling one’s own story.\textsuperscript{34} Concrete evidence for this has been given especially in writing about illness and traumatic events.\textsuperscript{35,36} Hatem and Rider, for example, cite clinical studies that show significant changes in physiologic parameters, such as improve-
ment of lung functions in asthma patients or decline of disease activity in patients with rheumatic arthritis due to writing about personal stressful experiences.\textsuperscript{37} Another study gives evidence about an increased immune response in Hepatitis B vaccinations in a group of medical students that wrote about a traumatic experience shortly before receiving the vaccination.\textsuperscript{38} Also talking about one’s experience has the potential to heal, as Pennebaker makes clear,\textsuperscript{39} because the expression of emotion can have a cathartic effect.\textsuperscript{39} And it ultimately helps all parties involved in developing their human potential: “narrative-based medicine is about helping people to tell stories that have to be told if all of us are to remain fully human.” Arthur W Frank concludes.\textsuperscript{40,41}

**Narrative in Medical Practice**

A narrative approach in medicine will only succeed if ultimately it has a positive effect on daily practice instead of just adding to already existing pressure. Thus, it is helpful to point out that complex illness narratives as published in biographies or collected by social scientists are useful for training and research purposes. The complexity of these published narratives is neither applicable nor necessary in daily medical practice.\textsuperscript{41} A narrative approach in daily medical encounters consists mainly of a specific openness towards patients and their narratives in the practice of medicine, using narrative skills, such as:

- Sensitivity for the context of the illness experience and the patient-centered perspective
- Establishing a diagnosis in an individual context, instead of merely in the context of a systematic description of the disease and its etiology
- Narrative communication skills, such as exploring differences and connections, hypothesizing, strategizing, sharing power, reflection active listening, and circular questioning (a technique originally from systemic family therapy aiming at a differentiated view on a specific topic; it can include questions that are ranking, speculative, relational or contextualizing)\textsuperscript{42,43,44}
- Self-reflection.

To use the potential of narratives for self-reflection and professional development, Gillie Bolton proposes reflective writing courses, where practitioners put their experience in words—even poetry—and reflect on them in a facilitated and mentored peer group.\textsuperscript{42,43}

Because the language and life-world of patients and physicians can be so far apart, it might be helpful to have an intermediary. Celia Engel Bandman encapsulates this position in her concept of a facilitator between the physician’s and the patient’s world that she calls a medical humanist.\textsuperscript{44} The term is derived from the philosophical tradition and worldview of humanism and is not to be confused with the field of the medical humanities. Ms Bandman’s role as a Medical Humanist in a cancer center in Vermont is to create a bridge between physician and patient:

“By recognizing that the language of medicine and the language of the patient’s world transformed by illness are not the same, the medical humanist creates a communication bridge. And in so doing, provides support to both doctor and patient as they face uncertainty.”\textsuperscript{45}

Ms Bandman, a writer who understands the impact of words and how language shapes experience, does this, for example, by helping patients to find words for their experience and to include them in the medical record: “The ‘Medical Humanist’s Note’ documented the patient’s story in their own words and was filed alongside the clinical record which made for the whole story” (Celia Engel Bandman, personal communication, 2003 Mar 23).\textsuperscript{42,43}

**Pitfalls of Narrative-Based Medicine**

Finally, some warning remarks might be appropriate. NBM is not all beer and skittles. It takes time and effort because “significant technical and attitudinal change that is necessary does not come quickly.”\textsuperscript{46,47} At the beginning, embarking on the narrative adventure can lead through a phase of destabilization and doubt about one’s own approach to medical practice. It can also lead to a phase of getting carried away by it. “The biggest challenge in taking a narrative approach is knowing when to stop. Disease, disability, deprivation, and death are not stories. They are facts. Professionals, who get carried away by narrative ideas to the point where they forget this, are not safe.”\textsuperscript{46,47} Narrative is not the only thing that counts in medicine; by no means is it meant to devalue medical knowledge. Also there are patients who are not interested in telling their story or sharing their innermost feelings, and not every topic raised in a consultation calls for detailed narrative exploration.

The insight into the potential of narratives is not new, but it is necessary to re-enliven it: to find ways...
and forms to share stories and the personal experience of being ill and caring for the ill, and thus make a contribution to humanizing health care and encouraging individual personal growth, for the patients, the caregivers, and those who are still healthy.

\* Celia Engel Bandman, founder of the Centre for Communication in Medicine, Bennington, VT.

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**References**


Respect

Their story, yours and mine—it’s what we carry with us on this trip we take, and we owe it to each other to respect our stories and learn from them.

—William Carlos Williams, 1883-1963, physician and poet
Introduction

The rapidly increasing racial and ethnic diversity among Kaiser Permanente (KP) membership mirrors the demographic changes across the nation (Lynette DeSantis, personal communication, 2008 Nov). This diversity calls for interventions that are culturally specific to improve patients’ health outcomes and to eliminate health disparities (see Kaiser Permanente Diversity Demographics). This need is unequivocally demonstrated by scientific evidence that shows differential disease prevalence between population groups. The impact of disparities and the human story is repeatedly told in the reports that prompted the creation, in 1999, of The Office of Research on Minority Health and, in 2000, the Culturally and Linguistically Appropriate Services Standards (CLAS); in the Institute of Medicine’s 2002 report, Unequal Treatment: Confronting Racial and Ethnic Disparities in Health Care; and in the Annual 2007 National Healthcare Disparities Report (NHDR) by the Agency for Healthcare Research and Quality. Despite these significant efforts, disparities have not been reduced since the first NHDR in 2003.

During the 1990s, frameworks emerged to reverse health-disparity trends—a complex process. In particular, the practice-based, community-informed approaches to health and health care—that placed culture in the nexus of essential elements for solving health disparities—created a rich body of experience and examples now known as the discipline of culturally competent care. By 1998, the KP National Diversity Council, on the basis of the ever-growing body of knowledge and practice, began integrating these principles through a deliberate, research-driven strategy. KP membership data, health-disparities data, and the organization’s mission and purpose required a breakthrough to address differential population health outcomes. The Centers of Excellence are an innovative and specific response to these imperatives.

History and Strategy

In 1999, the Centers of Excellence in Culturally Competent Care concept was created through sponsorship of the National Diversity Council. The Centers’ purpose was to demonstrate the practical dimensions of population-based health issues with respect to culture, race, and ethnicity, written into the original National Diversity Culturally Competent Care Provider Handbook series. The Institute for Culturally Competent Care (ICCC) emerged shortly thereafter as an oversight body for the anticipated proliferation of Centers across the Program.

Now almost a decade later, the ICCC, a unit of Kaiser Permanente’s National Diversity Department, guides the work of nine Centers of Excellence in Culturally Competent Care within KP (Table 1) in collaboration with the respective facility Medical Directors and Administrators. The Centers demonstrate that skilled staff who respectfully explore issues of culture, race, and ethnicity during the patient’s point-of-care contact, can make an important contribution to positive patient health outcomes and reduce racial and ethnic health disparities. The Centers’
population-based, data-driven, research projects move in the direction of unraveling and explaining the dynamic positive and negative processes by which culture, race, and ethnicity interact in health care delivery settings to impact patient health outcomes.

Given the urgent national need to reduce health disparities, Centers will rededicate their efforts to demonstrate the universal applicability of respectful patient-centered, culturally skilled, quality care, which is at the heart of cultural competence. This contemporary, research-driven strategy coincides with those of multiple national organizations, guiding the intellectual and practical deliverables required to combine the agendas of quality, service, community participation, social determinants of health, disparities, cultural competence and health outcomes research.

The Center Story:
Practice and Potential

Three principles guide the work of the Centers of Excellence in Culturally Competent Care Initiative (see Sidebar: Center Principles). Each Center addresses health and health care disparities from the culturally specific view of a given population group: African Americans, Armenians, Latinos, persons with disabilities, and women. Taken together, the health foci include: cardiovascular disease, stroke, hypertension, prostate cancer, sickle cell disease, mental health, asthma, diabetes, obesity, spinal cord and brain injury, patient and provider education, translation and interpretation services, and culturally competent, cross-cultural patient-clinician communication.

The stories of four Centers are told below as illustrations of how the strategy and the principles operate in the Centers’ work.

1. The Kaiser Foundation Rehabilitation Center

The Kaiser Foundation Rehabilitation Center (KFRC) at the KP Medical Center in Vallejo, CA has provided care for patients with disabilities since 1946. This 60-bed inpatient rehabilitation hospital and outpatient center is accredited by the Commission on Accreditation of Rehabilitation Facilities.

The Center of Excellence for persons with disabilities at KFRC (demonstrating Principle 1) was founded in 2001 and is well known nationally and internationally for providing expert, interdisciplinary rehabilitative care to survivors of stroke, spinal cord injury, brain injury, and other disabling conditions.

In collaboration with the University of Washington, in Seattle, WA and with funding from the Centers for Disease Control, the Center examines how demographic and socioeconomic patient characteristics influence rehabilitation care following stroke to determine if disparities exist in the population under study. This Center works to unravel the details that contribute to the disparity in treatment protocols and care outcomes, based on place of treatment, and to

| Table 1. Centers of Excellence and their locations |
|-----------------------------------|--------------------------|
| **Center**                        | **Location**             |
| Center of Excellence in African-American Health | West Los Angeles, CA |
| Center of Excellence for Armenian Health      | Glendale, CA             |
| Latino Center of Excellence (LaCE)          | Denver, CO               |
| Center of Excellence for Persons with Disabilities at the Kaiser Foundation Rehabilitation Center (KFRC) | Vallejo, CA |
| The Colorado African-American Center of Excellence (AACE) | Denver, CO |
| Latino Center of Excellence (MAS-LCE)        | Baltimore, MD            |
| African-American Center of Excellence      | Cleveland, OH            |
| Center of Excellence For Women’s Health     | Fremont, CA              |
| Center of Excellence in Linguistic and Cultural Services | San Francisco, CA |

Center Principles

1. Contribute new knowledge through population-based research that provides compelling evidence about how culture, race, and ethnicity affect health outcomes in the clinical setting.
2. Disseminate, within and outside of Kaiser Permanente, advances in clinical practice, program expertise and innovations that offer contributions to the reduction and elimination of health disparities.
3. Apply the principles and practice of cultural competence, cultural humility, and cross-cultural communication in health care and health care delivery.
understand the characteristics of patients more likely to be referred to nursing homes. KFRC’s efforts to identify disparities and barriers to care for people with disabilities will assist the Kaiser Foundation Health Plan in directing programs and resources to improve care to members with disabilities.

2. Latino Center of Excellence, Denver, Colorado

Launched in 2001, the Latino Center of Excellence (LaCE) Denver, CO, (demonstrating Principle 2) focuses on achieving improved outcomes for Latinos by attaining higher efficiencies in care delivery, by developing greater capacity to treat increased demand, and by developing replicable delivery models in diabetes care. In 2006, LaCE implemented KP’s aspirin, lisinopril and lovastatin (ALL) protocol—a cardiovascular risk reduction strategy that focuses on maximizing prevention for those most at risk—to address disparities in cardiovascular disease among Latino patients with diabetes. The specific challenge was to adapt a KP population management strategy to the needs of Latino patients. The initiative used the tripartite medication regimen for Latino patients, over age 55 years with CAD and/or diabetes, and developed a culturally appropriate outreach intervention that included:

- an interdisciplinary, Spanish-speaking, primary care team of bilingual physicians, charge nurses, and medical assistants
- simplified Spanish instructions (“just take these three pills each day”) to increase adherence amidst varying health literacy levels
- communicating instructions in Spanish
- bundling fixed doses of the three medications so that one visit could accomplish what often took many visits using only generic or inexpensive medications
- active follow-up with trained members of the health care team; and
- minimizing redundant and unnecessary laboratory tests.

The indicator of ALL medication pick up (medication “adherence”) was one benchmark of improvement, along with the percentage of those patients having an eye exam and HbA1c tested in the previous 12 months, and reaching the target goal of LDL levels less than 130mg/dL.

“The ALL Initiative” (aka “PHASE” in the KP Northern California Region) is in operation in all KP regions, and is also being supported among KP’s “safety net” partners—organizations outside the KP system that serve a disproportionate number of underserved and minority populations.

3. The Women’s Center of Excellence

Started in 2002, this Center (demonstrating Principle 3), which is located in Northern California, houses the Diversity, Data and Demographics Program (DDDP). This innovative, replicable, and culturally sensitive patient and physician satisfaction evaluation method was adopted and implemented at the Center in 2005. The DDDP provides physicians with culturally specific data regarding their patient profiles in an effort to improve the patient care experience and quality outcomes. The increase in physicians’ understanding of their patients’ needs results in increased patient-physician communication, strengthens the patient-physician relationship, patient satisfaction in quality of service, and physician satisfaction in their work.10,12 This evaluation method identifies culturally complex issues at the individual, departmental, and facility level resulting in unique solutions that are easy to implement, with demonstrated improvement in three months through educational interventions and physician coaching. As importantly, physician satisfaction scores improved along with physician retention, especially among women and bilingual physicians. Over 150 physicians participated in this process. Notably, the DDDP originated from an individual Ob/Gyn physician’s reflection on his own patient satisfaction data, which showed increased patient satisfaction with older female patients than with younger women, ages 18-35 years.

The Women’s Center of Excellence DDDP approach to culturally contextualizing the patient and physician’s approach has a potentially large positive impact on the business success of the organization by specifically responding to the needs of an increasingly diverse population at the point of the clinical encounter.

4. The Latino Center of Excellence Mid-Atlantic States

Since July 2007, the Latino Center of Excellence (LCE) in the Mid-Atlantic States (MAS) has provided culturally competent and linguistically appropriate
services and resources to Latino patients. The LCE goals are to optimize Latino members’ health outcomes, to improve their compliance with medical recommendations, and to increase satisfaction with services. This is accomplished by:

- training staff through the KP Qualified Bilingual Staff program
- maximizing the use of the comprehensive HealthConnect asthma template by clinicians
- offering Spanish-language asthma education guides and classes
- creating patient asthma action plans at the time of the clinical encounter in the preferred language of the patient; and
- meeting language-appropriate signage and telephone language-line requirements at all service locations.

LCE offers its services in four MAS Medical Centers: Gaithersburg, Germantown, Loudoun County and Prince George’s County.

This Center’s research focus combines the elements of recording baseline information with regard to Latino patients and asthma, introducing interventions and measuring what change there is, if any, in patient outcomes. Some areas included in this multilevel investigation are: physician knowledge about current asthma protocols, treatment, and practice; cultural considerations when working with Latino families; language differentials between patients and providers; the influence of IT systems on care outcomes; and interventions such as bilingual- and Spanish-only asthma educational guides and classes. This Center will provide rich practical data applicable to Latino patients with asthma, and undoubtedly, will reveal lessons for all KP patients.

**Research and Evaluation**

Inherent in the structure of the Centers of Excellence is an evaluation component based on each Center’s formal agreement to provide culturally specific, evidence-based practice, consistent with the strategy and principles. Each Center signs a Memorandum of Understanding in which the proposed cultural intervention is evaluated as a research project, complete with data collection, analysis and reporting methods that will advance the field of knowledge and practice in eliminating health care disparities. In this regard, the evaluation methods include ways to uncover, and give language to the processes that create successful outcomes, and also what limits success. The biyearly site-visits to the Centers by the Director of the IC CC serves as a quality control mechanism, engaging Center leads, researchers, clinicians and staff in an active, relationship-based, close review of benchmarks and deliverables. An overall evaluation for the Centers is in development, and a schema will be completed by 2009.

**Sustain and Transfer**

The nine Centers of Excellence in Culturally Competent Care show great promise (Table 1). Locally, Centers engage in a unique community health partnership giving clinicians the opportunity to enhance their skills. Regionally, Centers recount promising, population-based health models and lend strength to the business case for recruiting and retaining a diverse membership—through services that indeed support positive health outcomes and health status. Across the regions, Centers are well positioned to disseminate and replicate successful programs, to demonstrate cost effectiveness and equity in the standard of care, and to contribute culture-specific methods for reducing health disparities. The KP Health Disparities’ Vision/Strategy Statement, in the tradition of Sidney Garfield, MD’s visionary care, states:

“Kaiser Permanente will be a leader in eliminating disparities in health and health care. We will do this by providing equitable care to our members, targeting resources to areas of need in the communities we serve, and identifying and implementing strategies and policies that support equity in health nationwide, including universal health coverage.”

This strategic commitment from the national level and from the highest officer in the organization reinforces the importance placed on the Centers of Excellence as models within the organization where this commitment is advanced and actualized. In addition, KP intends to open at least two new Centers next year, with start-up funding from the National Diversity Council. Plans for the Center of Excellence in Childhood Obesity, Pacific Northwest and for a Center focused on the Asian-American population are under discussion. Sustaining the Centers requires capable leadership, adequate personnel, and the ability to integrate the culturally competent care concept across KP operations. Plans for publishing the results from the Centers of Excellence research and activities in peer-reviewed
journals are underway. Given KP’s prominence in the health care industry, we expect that the lessons, which include the successes and limitations of the Centers’ research and initiatives, will inform the work of many constituents in health care and health care delivery.

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References
17. The Lewin Group Inc. Community participation can improve America’s public health systems [monograph on the Internet]. Battlecreek (Mi); WK Kellogg Foundation; 2002 Apr [cited 2008 Jun 2]. Available from: www.wkkf.org/Pubs/Health/TurningPoint/Pub3713.PDF.
Tribute to Robert Hippen, MD

“How’s it goin’ señor?”
those words indelible
in my memory of the man
that I am now forced
to say goodbye to.

It is not fair that I shall
never again critique a new poem,
that I will not see him
in another Tuba Christmas
or across the battlefield
of a hardy RISK game.

I want the chance again
to discuss work
or life in general,
R Crumb,
or jazz,
but I am denied.
His wit and insights
are gone from me forever —
and sadness fills the void.

Editor’s Note
Robert Hippen, MD, was a long-time Northwest Permanente Radiologist at the Skyline Medical Center in Salem, OR. Dr Hippen passed away suddenly in early September. He is survived by his wife and son. Dr Hippen was a member of The Permanente Journal Review Board for many years and a frequent contributor to the Soul of the Healer—his contributions will be missed. A colleague of Dr Hippen wrote this tribute in his honor. Following are two poems Dr Hippen had submitted recently that had yet to be published.
Honorable Mention

Robert Hippen, MD

On her good days she might apply a little make-up, as if she had someplace to go, and cared.

On those days she would wear the diamond studs and the morning rose up like fire in her cheeks.

“Legs still strong,” she would say, and talk about her day, which was like most days, and each day she expected I would arrive, and most often I did, though it was over ten years since her eyes first called me to her fallen breasts, and sometimes I doubted I would ever return.

Whether she had wanted children, or had them and gave them up, or why she didn’t marry, I never knew, and me a family man.

In those days there was a chill to her rooms that even her thin smile could not remedy, so mostly she just sat there and waited it out.

And all that time she could not recall why she had first asked me to come; over ten years gone by, and still the old girl did not remember my name.

Old Man Waiting at a Bus Stop

Robert Hippen, MD

The bent figure, black hat tilted down, rain dripping off the brim, back to the wind.

You’ve been waiting like this most of your life, worried you would miss it, worried it would come.

Now you pause and hold your breath. The headlights a faint glimmer … will you sing hallelujah, dance in a puddle one last time?
It was an inauspicious beginning—as it would have been for any new physician, let alone a young man of great vision and ambition. The year was 1933, four years into the desperation of the Great Depression. Sidney R Garfield, having completed his surgical residency at Los Angeles County General Hospital, launched his medical career by leaving the growing metropolis and constructing a compact, 12-bed hospital in the southern end of the desolate Mojave Desert east of Los Angeles. His father, Isaac, helped the 27-year-old with a $2250 loan, about $35,000 in today’s dollars. His prosaically named Contractors General Hospital, a mile or so off the then new, two-lane transcontinental US Highway 60, was about halfway between Los Angeles and Phoenix. The nearest town, a roadside outpost called Desert Center, was about six miles to the east. The locale, as described by one observer, was a “hot, dusty region never meant by God for human activity or habitation.”

With jobs almost impossible to find, even in medicine, Garfield looked to this remote spot when he learned about construction of the Metropolitan Water District of Southern California’s aqueduct designed to bring Colorado River water to Los Angeles. Thousands of men were laboring under dangerous and physically demanding conditions in the harsh desert environment. Garfield reasoned they would need on-site medical care.

Desert Center had been founded about a dozen years earlier by an itinerant preacher and cotton farmer at a spot where his car had broken down. It was an aptly named dusty and lonely wide spot on the highway where a traveler could get a meal at the 24-hour café, buy gas, and refill the canvas water bags to use if the car engine overheated while crossing the desert. It was about 50 miles east of Indio, the largest city in the region where Dr Gene Morris, former intern at Los Angeles County Hospital, had grown up and had returned to set up a medical practice. Morris told his friend Garfield about the construction project with thousands of aqueduct workers covered by California’s progressive system of workers’ compensation, but with no medical or hospital care available near their work camps. The two young doctors formed a partnership and built their wood-frame hospital on the edge of a construction camp. Garfield named it Contractors General Hospital and ensured that it was modern and well-equipped with creature comforts, including air conditioning—an innovation installed in the White House in 1930 but not in widespread use, especially not in rural hospitals.

With 5000 aqueduct construction workers now at jobsites spread across 150 miles of desert, getting patients, they figured, would not be a problem. The two young doctors were gambling that on-the-job injuries alone would bring them plenty of patients insured for industrial accidents—enough to make the hospital an economic success. They were right. Men suffering from on-the-job injuries did come, but Contractors General tended to get only the relatively minor cases. Insurance companies shipped serious cases—the ones that provided the most significant income—to hospitals in Los Angeles. To make matters worse, the insurance companies discounted the physicians’ bills for the care...
they did give, claiming they overtreated patients. “We got a patient,” Garfield explained, “and we would treat him with tender loving care and we would bill the insurance company, and more often than not, they would come back and discount our bills, saying that we treated the patient too many times.” Even when the insurance companies did pay, they were slow in paying.

Another problem arose when the aqueduct workers came in with all sorts of illnesses clearly not covered by their workers’ compensation insurance, including venereal diseases from prostitutes who also set up shop near the work camps. That would not have been a problem, except that few of the men could pay their medical bills. The cost of treating nonpaying patients soon put a major financial strain on the busy little hospital. Discouraged, Dr Morris sold his share of the partnership to Garfield. Garfield was now on his own, with just one nurse, a housekeeper/cook, and her husband, who served both as orderly and ambulance driver.

As if nonpaying patients, slow-paying insurers, rattlesnakes, scorpions, and scorching summer temperatures that rarely dipped below triple digits were not discouragement enough, a new threat to his struggling enterprise arose. One day a sedan turned off Highway 60 in a cloud of dust and headed up the dirt road toward Contractors General. Two men got out and identified themselves as representatives of a finance company. They had come to seize Garfield’s Ford panel truck, which had been outfitted as an ambulance.

Garfield had not been able to afford an ambulance, and a local undertaker in Indio had offered him a deal: He would rent the ambulance to Garfield for $25 a month if Garfield would help him get undertaking work from the aqueduct project. But after more than a year, there had been few deaths. The unhappy undertaker wanted out of the ambulance lease, so he went to a finance company in nearby Riverside, took out a loan using the ambulance as collateral, and then neglected to make the payments. When the finance company complained, he told them to repossess the ambulance. But they reappeared two days later with the county sheriff, who carried a warrant for Garfield’s arrest for assault with a deadly weapon. The sheriff, a good friend of Garfield’s, explained he had no choice but to take Garfield to jail because of the warrant. His plight had gone from bad to worse. The ambulance was gone, and Garfield, if convicted of assault with a deadly weapon, could lose his medical license.

Fortunately, he rejected his first attorney’s advice to plead guilty and pay a fine. With a second attorney, he instead went to trial and won a not-guilty verdict. But being found not guilty was not enough for Garfield, whose honor and reputation were at stake. He sued the undertaker, the finance company, and their attorney for malicious prosecution and won. He was awarded $3000, a portion of which he promptly used to finance a new ambulance.

The ambulance incident was, in some ways, emblematic of the first phase of Garfield’s extraordinary career—the daring desert years of creating something from nothing, of struggling against daunting odds to achieve his ends. Given his determination to succeed, whatever the obstacles, he exhibited a characteristic refusal to allow second thoughts to give him pause. Indeed, Garfield, in these early years, had a vague sense of struggling against daunting odds to achieve his ends. Given his determination to succeed, whatever the obstacles, he exhibited a characteristic refusal to allow second thoughts to give him pause. Indeed, Garfield, in these early years, had a vague sense he was working toward something larger than personal success. Today, across the road from old US Highway 60 and the still operating Desert Center Café, where Garfield could celebrate his legal victory with a 50-cent roast beef dinner, stands California Historical Marker No. 992, in Garfield’s honor, to announce to occasional visitors that something very special and enduring was born in this lonely corner of the desert.
PERIOD. A Girl’s Guide
by JoAnn Loulan and Bonnie Worthen
Illustrated by Chris Wold Dyrud and Marcia Quackenbush

By Karen Azani

When I first opened the pages of \textit{PERIOD. A Girl’s Guide}, I was hesitant to revisit the days of my first experiences with puberty. But this book exceeded my expectations and made even the most uncomfortable topic easy to read. \textit{PERIOD. A Girl’s Guide} discusses everything a young woman needs to know as her body undergoes various changes. There is nothing left out, from diagrams of a woman’s body to the first visit with a gynecologist.

I was most impressed by the manner in which the information is brought about. The words are not too complex but at the same time, I did not feel like I was reading a book for six year olds. The most important thing for many young women when learning about menstruation is the need to feel mature. This book delivers the necessary information in a tone meant for young adults. Furthermore, the book found the happy medium between too much information and not enough detail. For example, the pictures were not too revealing and gave me a general idea. I was also pleased that this book touched on a significant issue: everyone is different. I was worried when I was younger about getting my period later than many girls my age. This book assures girls that it is okay to be different because everyone’s bodies mature at different times.

I enjoyed reading \textit{PERIOD. A Girl’s Guide} and I wish that I had read it when I first experienced menstruation. It is important that every young woman understand what her body is going through, and this book succeeds in answering many essential questions. I would definitely recommend this book to any young girl; moreover, I would recommend it to all women who would like to know more about how our bodies work.

Prime Matter

… for the natural substance of the menstrual fluid is to be classed as “prime matter.”

—Aristotle, 384-322 BC, Greek philosopher