Hyperglycemia and Switching to Subcutaneous Insulin

The Case

A 47-year-old man with type 2 diabetes was admitted to the hospital with nonketotic hyperglycemia due to medication nonadherence. He was placed on a transitional care (step-down) unit and the decision was made to start an intravenous (IV) insulin drip to control his hyperglycemia. This hospital used the Glucommander—a computer-based system that recommends insulin and IV fluid infusion rates based on the patient's blood glucose levels—for protocol-based management of hyperglycemia. The admitting physician entered initial orders into the Glucommander, and the system recommended changes to the infusions based on subsequent blood glucose measurements. Within several hours, the patient's blood sugars improved from over 600 to less than 200, so, per the protocol, his insulin infusion was decreased and the IV fluids were changed to D5 1/2 NS (hypotonic saline with added dextrose).

That evening, the patient began to experience chest pain. An electrocardiogram (ECG) was performed and showed T-wave inversions in the lateral leads, prompting concern for cardiac ischemia. The cross-covering resident and attending saw the patient and decided to transfer him to the intensive care unit (ICU) for closer monitoring. The patient was made NPO (nothing by mouth) in case an urgent cardiac procedure was required. The resident therefore decided to discontinue the Glucommander, as he did not want the patient to experience dangerously low blood sugars. Orders were written for the patient to receive sliding scale subcutaneous insulin, and his IV fluids were changed to normal saline with no added dextrose.

The patient's chest pain quickly resolved and he had no further ECG changes or evidence of cardiac ischemia. However, over the next several hours, the patient developed hyperglycemia, with blood sugars over 400. When the primary physician saw the patient the next morning, she realized that although normal protocol called for starting subcutaneous insulin 2 hours prior to discontinuing IV insulin, the patient actually did not receive any subcutaneous insulin until more than 2 hours after the infusion was stopped. As a result, the patient's blood sugars rapidly rose. This required him to remain in the ICU for an additional day in order to adequately manage his hyperglycemia, and led to a longer hospital stay. On review of the incident, the resident admitted that he had never actually transitioned a patient off the Glucommander to subcutaneous insulin, and the ICU nurse also had limited experience with this technology.

Managing Ascites: Hazards of Fluid Removal

The Case

A 50-year-old man with longstanding alcoholic cirrhosis presented to the emergency department (ED) with several days of progressive abdominal pain and worsening distension. He had no fevers or other infectious symptoms, bleeding, or recent changes to his medications. He also reported that his last drink was more than a year ago, reflecting a behavior change motivated by his desire for liver transplant consideration. In the ED, he was afebrile with normal vital signs and no evidence of jaundice. His abdominal exam was notable for marked distension with a fluid wave and a bedside ultrasound that confirmed significant ascites. The patient last required a paracentesis several months earlier for similar symptom relief. His laboratory results were notable for a stable anemia, a low platelet count of 50, an elevated INR of 2.5, and a mild transaminitis and leukocytosis. In the ED, his working diagnosis was acute decompensation of cirrhosis without a clear etiology.

Eager to relieve his symptoms, the providers performed a large volume paracentesis. While there was discussion about "how much to take off," the patient became acutely hypotensive as the 10th liter of fluid was being removed. The hypotension failed to respond to initial fluid resuscitation, and the patient

required a short duration of vasopressors in the intensive care unit before being weaned off. He was ultimately discharged after a 3-day hospitalization with an increase in his outpatient diuretic regimen and close follow-up in the liver clinic. The case prompted a formal review since the entire hospitalization was deemed preventable given the belief that his hypotension was a direct result of the aggressive fluid removal attempts.

Harm From Alarm Fatigue
Case & Commentary Part 1

A 54-year-old man with hypertension, diabetes, and end-stage renal disease on hemodialysis was admitted to the hospital with chest pain. His initial electrocardiogram (ECG) showed no evidence of significant ischemia, but cardiac biomarkers (troponin T) were slightly positive. He was admitted to the observation unit, placed on a telemetry monitor, and treated as having a non-ST segment elevation myocardial infarction (NSTEMI).

Overnight, the patient's telemetry monitor was constantly alarming with warnings of "low voltage" and "asystole." The bedside nurse initially responded to these alarms, checking on him several times and each time finding him to be well. The resident physician responsible for the patient overnight was also paged about the alarms. He came and checked the patient and the alarms and was not concerned. Both clinicians felt the alarms were misreading the telemetry tracings.

The scenario described in this case is common—skilled and well-intentioned health care providers diligently respond to repeated false alarms. Yet excessive false alarms may lead to unintended harm. This case provides an opportunity to consider the benefits and potential harms associated with the multitude of alarms in the hospital setting.

For many reasons (as in this case example), hospitalized patients are often monitored using telemetry. Unlike bedside ECG monitors in the intensive care unit where data is displayed in the patient's room, telemetry ECG systems transmit the ECG signal wirelessly to a central monitoring station where data for all of the patients is displayed. Some hospitals choose to utilize monitor watchers to identify alarms and notify nurses. Other hospitals use pager systems or enhanced sound systems on the unit to alert nurses to alarms. Since one monitor watcher is responsible for watching as many as 40 patients' data, only one ECG lead is typically displayed for each patient so that all patients' data can fit on one or two display screens.

While a standard diagnostic ECG acquires data from 12 different leads (via 10 electrodes placed on the patient's body), telemetry monitoring systems typically acquire data from fewer leads (via 3–6 electrodes placed on the patient's torso). One reason computer algorithms from telemetry monitoring systems are less diagnostic and less accurate than computer interpretations from the standard 12-lead ECG is that a limited number of leads (typically, 1–2) are used for analysis. If the telemetry algorithm uses just one ECG lead for analysis, this can more easily be misinterpreted, leading to false alarms.

Despite harnessing advanced technology, telemetry monitoring devices often misidentify heart rhythms as asystole. In this case, the providers were correct in concluding that the telemetry monitor device was misreading the patient's heart rhythm because a true asystolic event would have been clinically apparent. The most common cause of false asystole alarms is under-counting of heart rate due to failure of the device to detect low-voltage QRS complexes in the ECG leads used for monitoring. This patient's telemetry device warned of this problem with "low voltage" alarms.

After the nurse responded to these alarms by checking on the patient (multiple times) and contacting the responsible physician, the correct action would have been to search for another ECG monitoring lead with

greater QRS voltage. For example, the resident and nurse could have checked the patient's full diagnostic standard 12-lead ECG to determine which of the 12 leads had the greatest QRS voltage, and then changed the telemetry monitor lead accordingly. This may have prevented the repeated alarms that were a consequence of a low-voltage QRS.

In our recent study of alarm accuracy in 461 consecutive patients treated in our 5 adult intensive care units over a 1-month period, we found that low-voltage QRS complexes were a major cause of false cardiac monitor alarms.(1) The Figure shows the standard diagnostic 12-lead ECG of the single outlier patient in our study who contributed 5,725 of the total 12,671 arrhythmia alarms (45.2%) analyzed. Similar to the case described here, under-counting of heart rate due to low-voltage QRS complexes led to repetitive false asystole alarms in our patient.

Case & Commentary Part 2

The nurse and resident decided to silence all of the telemetry alarms (in this observation unit, there was not continuous or centralized monitoring of telemetry tracings). The patient was not checked for approximately 4 hours.

When the bedside nurse went to perform the patient's morning vital signs, he was found unresponsive and cold with no pulse. A code blue was called but the patient had been dead for some time. The cause of death was unclear, but providers felt the patient likely had a fatal arrhythmia related to his NSTEMI.

Silencing all telemetry alarms in this patient was an error that contributed to this patient's death. This patient was at risk for developing a fatal arrhythmia due to his acute myocardial infarction and co-morbid conditions (diabetes, end-stage renal failure). The arrhythmia would likely have triggered an appropriate alarm had the alarms been functioning, and the patient might have been saved. This adverse event reveals a clear hazard associated with hospital alarms. It also provides an opportunity to consider why such harms exist and what can be done to mitigate them.

What types and numbers of alarms occur with hospital monitor devices and how accurate are they?

Typically, there are three types of alarms generated with hospital monitor devices: *arrhythmia alarms* that detect a change in cardiac rhythm; *parameter violation alarms* that detect when a vital sign measurement (heart rate, respiratory rate, blood pressure, SpO_2, etc.) exceeds the "too high" or "too low" alarm limit settings; and *technical alarms* that indicate poor signal quality (e.g., a low battery in a telemetry device, an electrode problem causing artifact, etc.).

Because monitor manufacturers never want to miss an important arrhythmia, alarms are set to "err on the safe side." As a result, the sensitivity for detecting an arrhythmia is close to 100%, but the specificity is low. That is, arrhythmia alarms are programmed to never miss true arrhythmias, but as a consequence they trigger alarms for many tracings that are not true arrhythmias, such as when a low-voltage QRS complex triggers an "asystole" alarm. In our recent analysis of monitor alarms in 77 intensive care unit beds over a 31-day period, there were 381,560 audible monitor alarms, for an average alarm burden of 187 audible alarms/bed/day.(1) Of the 12,671 arrhythmia alarms that were annotated, 88.8% were false alarms and did not signify true arrhythmias.(1)

What is alarm fatigue?

Alarm fatigue occurs when clinicians become desensitized by countless alarms, many of which are false or clinically irrelevant. The development of alarm fatigue is not surprising—in our study, there were

nearly 190 audible alarms each day for each patient.(1) If only 10% of these were true alarms, then the nurse would be responding to more than 170 audible false alarms each day, more than 7 per hour. Consequently, rather than signaling that something is wrong, the cacophony becomes "background noise" that clinicians perceive as part of their normal working environment.

Patient safety concerns surrounding excessive alarm burden garnered widespread attention in 2010 after a highly publicized death at a well-known academic medical center.(2) Despite repeated low heart rate alarms before the patient's cardiac arrest, no one working that day recalled hearing the alarms. In the investigation that ensued, the Centers for Medicare & Medicaid Services (CMS) reported that alarm fatigue contributed to the patient's death.(3)

In the present case, clinicians turned off all alarms. Clinicians who find constant audible or textual messages bothersome may silence alarms at the central station without checking the patient or permanently disable them. Warnings have been issued about deaths due to silencing alarms on patient monitoring devices.(4) Moreover, several federal agencies and national organizations have disseminated alerts about alarm fatigue. In 2015, for the fourth consecutive year, ECRI listed alarm fatigue as the number one hazard of health technology.(5) In 2013, The Joint Commission issued an alarm safety alert (6); they established alarm safety as a National Patient Safety Goal in 2014, with further regulations becoming mandatory in 2016.(7)

Why is alarm fatigue dangerous?

The biggest harm that can result from alarm fatigue is that a patient develops a fatal arrhythmia or significant vital sign abnormality that is not noticed by the clinical staff because that patient's heart rhythm monitor has been plagued with false alarms. Imagine a neighbor who has a hair trigger car alarm that goes off all the time. If someone actually breaks into this car, setting off yet another alarm, would anyone be likely to call the police?

A number of different forces result in an excessive number of cardiac monitor alarms. The key contributing factors are (i) alarm settings that are not tailored for the individual patient (i.e., leaving hospital default settings in place even if they don't make sense for an individual patient); (ii) the presence of certain patient conditions such as having low ECG voltage, a pacemaker, or a bundle branch block; and (iii) deficiencies in the computer algorithms present in the devices.

What can be done to combat alarm fatigue?

Many steps can be taken to combat alarm fatigue and ensure that alarms that truly indicate a change in condition are responded to in an appropriate manner. First, devices themselves could be modified to maximize accuracy. One example would be to build in prompts for users. For instance, in patients with persistent atrial fibrillation (an irregular heart rhythm that can trigger telemetry alarms) rather than have the alarm repeatedly triggering in response to the atrial fibrillation, the monitor could generate a prompt, "do you want to continue to hear an atrial fibrillation alarm?" Another suggestion for industry is to create algorithms that analyze all of the available ECG leads, rather than only a select few leads. This could minimize the number of false alarms for asystole, pause, bradycardia, and transient myocardial ischemia. Lastly, algorithms that integrate parameters (i.e., link heart rate and blood pressure) could help determine if alarms are real or false by checking to see if there was any simultaneous physiologic impact. For instance, an algorithm-defined asystole event that was not associated with a simultaneous drop in blood pressure would be re-defined as false and would not trigger an alarm.

In addition, individual nurses and providers at the bedside can take steps to improve the usefulness of alarms. First, nurses and providers can review their hospital alarm default settings to determine whether some audible alarms that do not warrant treatment can be changed to inaudible text message alerts. Furthermore, nurses can tailor alarm settings for individual patients because hospital default settings may not make sense for the individual patient. For example, if the hospital default setting for high heart rate is set at 130, but a certain patient with atrial fibrillation has a heart rate averaging 135, then to avoid incessant alarms the alarm threshold needs to be increased while treatment is underway.

Lastly, institutions can take steps to improve the use of alarms and combat alarm fatigue. Committees charged with addressing alarm management should be formed and include all levels of the organization to ensure recommendations for practice changes can be carried out. We recently conducted a human factors analysis and determined that clinicians (nurses, physicians, and monitor watchers) found it difficult to respond to alarms or adjust alarm settings when working at the central monitoring station.(8) Importantly, most participants reported they had not had training on how to use the monitoring equipment. This highlights the need for education and training of all staff that interact with monitoring devices. Training should be provided upon employment and include periodic competency assessments.

An Obstructed View

The Case

A 66-year-old man with a history of benign prostatic hyperplasia and obstructive sleep apnea presented to the emergency department (ED) with subacute abdominal pain that had become much worse the previous evening. He reported relatively mild abdominal pain for the past 2–3 weeks, which was described as in his "mid-abdomen and crampy." The previous night, soon after eating dinner, he developed severe mid-abdominal pain that did not radiate and did not remit. He had never experienced abdominal pain of this severity. He reported no nausea, vomiting, diarrhea, fevers, chills, weight loss, or night sweats. He did report occasional constipation but had a normal bowel movement the day prior to presentation. The patient had never had a colonoscopy. On initial evaluation, the patient had stable vital signs, a tender abdomen without rebound or guarding, and unremarkable laboratory test results. A CT of his abdomen/pelvis noted mild dilation of the ascending, transverse, and proximal descending colon with associated air-fluid levels in the ileum and a possible "transition point concerning for stricture/mass or physiologic peristalsis."

Because the patient appeared well, he was admitted to the medicine (instead of surgery) service for observation, pain control, and serial abdominal exams. Surgical consultation was not requested at time of admission. Approximately 48 hours into the hospitalization, the patient's abdomen became more distended, with increased abdominal pain and tenderness with rebound on exam. A surgical consultation was requested. After the surgeons reviewed the imaging and performed a physical examination, they took the patient urgently to the operating room, where an obstructive mass with associated perforation was noted. The patient had a prolonged postoperative course with intra-abdominal infection before ultimately dying. The institution formally reviewed the case because of concerns regarding a possible delay in treatment and surgical consultation.

Amphotericin Toxicity

The Case

A 42-year-old woman status-post left pneumonectomy for aspergilloma was being treated with oral posaconazole for residual fungal disease. She presented to the outpatient infectious disease (ID) clinic with 2 weeks of pain, erythema, and purulent drainage around her sternotomy site. She was diagnosed

with sternal osteomyelitis with multiple areas of fluid collections, felt to be due to contiguous spread from her aspergilloma. After surgical debridement, tissue cultures revealed *Aspergillus fumigatus.*

Per ID consultation, the patient was switched from posaconazole to intravenous (IV) liposomal amphotericin B (Ambisome) for presumed posaconazole treatment failure. Hours into the IV infusion, the patient developed nausea, vomiting, diaphoresis, and rigors. The next morning, it was discovered that she had been given conventional amphotericin B (Fungizone) at the intended 5 mg/kg liposomal amphotericin B dose. When treating aspergillosis, conventional amphotericin is dosed at a maximum of 1–1.5 mg/kg. Thus, the administered dose represented a 5-fold overdose. The patient developed acute kidney injury, which subsequently subsided, and she ultimately was discharged home with IV caspofungin to finish her course of antifungal therapy.

Multiple factors contributed to this error. First, the resident on the consulting ID team, unfamiliar with the different formulations of amphotericin B, did not distinguish between the two preparations in his progress note. He wrote for "amphotericin B" in his note, while the attending ID note specified "Ambisome" at 5 mg/kg. The primary service (thoracic surgery) inadvertently prescribed conventional amphotericin B (Fungizone) at the ID consult–recommended dose of 5 mg/kg. Second, the electronic prescribing system lacked an alert for the conventional amphotericin formulation that would have notified the prescribing physician that the dose was out of the recommended range. Third, the pharmacist filling the prescription was also unfamiliar with the different amphotericin formulations and did not recognize the toxic dose, either while compounding the medication or sending it to the floor. Finally, the nurse administering the infusion (given during shift change) did not recognize that the patient was having an infusion reaction. Consequently, the infusion was allowed to run to completion. The dosing error was not identified until the next morning.

While not irreversibly harmed, the patient experienced an infusion reaction and acute kidney injury. Her hospital stay was extended for 3 extra days. She was discharged home with a PICC line for prolonged IV caspofungin therapy (a suboptimal antifungal agent for treating aspergillosis), due to her fear of receiving more amphotericin. Had she received the proper medication at the proper dose during her admission, she may have not needed the PICC line at all.

The Risks of Absent Interoperability: Medication-Induced Hemolysis in a Patient With a Known Allergy
The Case

A 47-year-old man with paraplegia (secondary to a gunshot wound) and a history of polysubstance abuse presented to the emergency department (ED) of Hospital Y late in the evening with pain and fever. The patient reported he had been to four different hospitals in the past few weeks and recently left against medical advice from Hospital X that morning to celebrate his birthday. Outside records from Hospital X obtained by the ED were scanty but revealed that the patient had presented with sepsis and had received antibiotics and intravenous fluids for presumed infection prior to leaving.

He was diagnosed, again, with sepsis secondary to sacral decubitus ulcers. He was given intravenous fluids, started on vancomycin and piperacillin-tazobactam, and admitted to the hospital for further management. During the day, he appeared to be improving on antibiotics. At approximately 3 AM, the patient was found unresponsive by his nurse. A code blue was called, and he was noted to be in PEA [pulseless electrical activity] arrest. He achieved return of spontaneous circulation after 4 minutes of cardiopulmonary resuscitation. He was intubated and transferred to the intensive care unit (ICU).

Upon arrival to the ICU, his hemoglobin was undetectable, and clinicians determined that the arrest was secondary to massive intravascular hemolysis (acute rupturing of his red blood cells). Based on the

clinical presentation, the hemolysis was presumed to have been caused by a reaction to the piperacillin-tazobactam.

The patient was transfused with 8 units of packed red blood cells and his hemoglobin improved. Unfortunately, his cardiac arrest led to an anoxic brain injury, and he remained in a vegetative state.

Later that day, previously requested records arrived from three hospitals where the patient had been cared for recently. One record revealed that he had experienced piperacillin-tazobactam–induced hemolysis last month, resulting in cardiac arrest and a 2-week ICU stay. This severe life-threatening allergic reaction was not known to any providers in the current hospital. On admission, the patient reported no allergies to medications, but he did state that he had "a reaction to a transfusion" where "my white cells were attacking my red cells and my heart stopped." In light of this answer (and the absence of data from the other hospitals), he was noted to have no medication allergies.

After 3 weeks in the hospital, the patient was transferred to a long-term care facility with a poor likelihood of recovery.

Dual Therapy Debacle

The Case

An elderly man with a history of arthritis, benign prostatic hypertrophy with urinary obstruction, hyperlipidemia, obesity, and a long history of tobacco use presented to a local emergency department for chest pain. An electrocardiogram revealed a new anterior myocardial infarction, and a cardiac catheterization confirmed single-vessel disease isolated to the left anterior descending artery. The resulting percutaneous coronary intervention (PCI) resulted in the placement of two drug-eluting stents. After stent placement, the patient was placed on triple anticoagulation therapy consisting of warfarin, clopidogrel (Plavix), and aspirin (ASA).

One month after placement, he received follow-up from a cardiologist and was informed he should remain on triple therapy for 6 months, at which time the warfarin would be discontinued. The plan was to continue the clopidogrel and aspirin (dual anticoagulation therapy [DAPT]) for an additional 6 months.

The patient saw his primary care provider (PCP) periodically over the next few years. These visits presented opportunities for his PCP to reconcile his medications. However, despite the plan to discontinue the DAPT after 1 year, the patient remained on this regimen 3 years after stent placement. On a preoperative visit for prostate surgery, he saw a cardiologist, who determined the patient had asymptomatic, stable coronary artery disease and affirmed his surgical candidacy. He further recommended discontinuing the clopidogrel, while continuing aspirin indefinitely. The cardiologist noted that an FDA Advisory Panel recommends just 12 months of DAPT after drug-eluting stent implantation, due to an increased risk of bleeding after 24 months of DAPT. The patient's PCP documented a telephone conversation with the patient in which he informed him to stop the clopidogrel and cleared him for prostate surgery. Nonetheless, the patient re-started the medication after the operation.

During yet another preoperative visit (this for removal of a skin cancer), it was discovered that the patient had re-started the clopidogrel. At this point, the clopidogrel was finally discontinued, and the PCP removed the drug from the patient's medication list in the electronic medical record.

A Fumbled Handoff to Inpatient Rehab

The Case

An 18-year-old man with no significant past medical history sustained a traumatic brain injury after a motor vehicle collision while driving intoxicated. The patient was admitted to a regional trauma center and required a decompressive craniectomy (removal of part of the skull bone) due to brain swelling as a result of his injury. He survived, but required prolonged care in the adult trauma intensive care unit (ICU).

His neurologic status remained poor, and he required a tracheostomy due to difficulty weaning from mechanical ventilation as well as placement of a percutaneous endoscopic gastrostomy (PEG) tube for nutrition. After a 3-week hospitalization the patient was transferred to a pediatric acute rehabilitation facility. He was scheduled to return to the trauma center for cranioplasty (repair of the skull defect) in 2 weeks. The plan was for him to continue to be weaned from the ventilator and receive physical and occupational therapy at the rehabilitation facility, likely for a period of several weeks to months.

The patient became increasingly agitated during his rehabilitation stay, and he eventually pulled on and broke his PEG tube. This necessitated a return to interventional radiology at the trauma center for removal of the retained PEG tube bulb. The patient was then admitted to the hospital for cranioplasty. He appeared to be doing well postoperatively and was transferred back to the pediatric acute rehabilitation center on postoperative day 2, which was a Friday afternoon.

The next day (Saturday), he had an acute change in mental status and new onset seizures. He was emergently transferred to the ICU at the pediatric hospital affiliated with the rehabilitation facility—not the adult facility where his surgeries had initially been performed. A stat head CT showed enlarged ventricles and a midline shift, indicating acute hydrocephalus (obstruction of the outflow of cerebrospinal fluid from around the brain). After realizing another surgical procedure would be needed, the patient was then transferred back to the trauma center, where an extraventricular drain was placed. After the procedure, the patient was then transferred back again to the rehabilitation facility, despite concerns on the part of the facility staff about the complexity of the patient's needs.

Abdominal Pain in Early Pregnancy
Case & Commentary—Part 1

A 34-year-old woman who was 14 weeks pregnant presented to the emergency department (ED) with 5 days of nonspecific abdominal pain, nausea, and vomiting. On examination, she appeared well with normal vital signs and had some mild diffuse abdominal tenderness. Her white blood cell count was 19,000 cells/μL, and a urinalysis was positive for nitrates and leukocyte esterase (indicating possible infection). She was diagnosed with a urinary tract infection and was discharged on antibiotic therapy. No imaging was performed at this initial visit.

The patient returned the following day with unchanged abdominal pain and more nausea and vomiting. A fetal ultrasound was performed and found normal fetal heart activity. No further testing was done, and she was discharged home with instructions to continue the antibiotics.

Abdominal pain remains the most common reason for emergency department (ED) visits, comprising more than 11% of all visits in 2008.(1) In 2011, 54% of patients that presented to the ED were female, more than 25% were of childbearing age, and the pregnancy rate in the United States is approximately 10% at any given time.(2,3) For these reasons, clinicians that evaluate patients with abdominal pain in the ED should be familiar with common causes of abdominal pain in pregnant women and appreciate when nausea and vomiting in pregnancy is abnormal.

Nausea, vomiting, and abdominal pain are very common in pregnancy. Up to 80% of pregnant women experience nausea and vomiting, most commonly in the first trimester. Symptoms and signs that may

indicate another cause include nausea and vomiting persisting past mid-pregnancy (approximately 20 weeks) and associated abdominal pain, fever, or diarrhea. In these instances, a more thorough evaluation is indicated.(4) Due to the enlarging uterus and fetal position/movement, abdominal pain is also common in pregnancy. Warning signs include pain that is localized, abrupt, constant, or severe, or pain that is associated with nausea and vomiting, vaginal bleeding, or fever. With any of these, further investigation into nonpregnancy-related causes is warranted. If any of the warning signs above is present, consultation with an obstetric specialist is recommended.

Women of childbearing age who present to the ED with abdominal pain at minimum should receive a urine pregnancy test, and the location and gestational age of the pregnancy should be determined with ultrasound. Miscarriage and ectopic pregnancy are the most frequent causes of abdominal pain in early pregnancy and are often accompanied by vaginal bleeding.(5,6) Once an early gestational age and intrauterine location is confirmed and miscarriage is ruled out, nonobstetric causes of abdominal pain should be explored, especially if any of the warning signs above are present.

With the exception of ovarian torsion, which is more common in the first trimester, the cause and incidence of non-obstetric abdominal pain in pregnancy varies little by gestational age of the fetus. The following are approximate incidences of some causes of acute abdomen in pregnancy: appendicitis (1/1500 pregnancies), cholecystitis, nephrolithiasis, pancreatitis, and small bowel obstruction (each occur in approximately 1/3000), with ovarian pathology (torsion or symptomatic masses) and uterine leiomyomas less common.(7)

After a history, physical examination, and the pregnancy test and ultrasound, laboratory tests that can assist in narrowing the differential diagnosis—including a complete blood count, liver and pancreatic enzymes, and urinalysis—should be reviewed. The white blood cell count increases to 10,000–14,000 cells/μL in normal pregnancy (and as high as 30,000 cells/μL in labor). However, a left shift in the differential and the presence of bands are abnormal and require further investigation.(8) If clinical signs and symptoms accompanied by laboratory data are not conclusive, prompt imaging may be necessary.

Imaging in pregnancy should begin with ultrasound or magnetic resonance imaging (MRI) as they have no ionizing radiation and have not been linked with fetal harm. Compression ultrasound may be useful in the evaluation of suspected appendicitis, cholecystitis, nephrolithiasis, and ovarian pathology in this setting. However, compression ultrasound becomes less sensitive and specific in pregnancy and relies heavily on the skill of the technician or radiologist. If the ultrasound is nondiagnostic, MRI can be considered as its lack of ionizing radiation also makes it safe for the fetus. MRI can aid in diagnosing acute appendicitis, cholecystitis, bowel obstruction, and ovarian pathology. If MRI is unavailable and there is serious concern for a nonpregnancy-related cause for the abdominal pain, computed tomography (CT) scanning can be performed.

If diagnostic tests that contain ionizing radiation (e.g., CT scanning) are deemed to be clinically necessary, they should not be withheld in the pregnant patient even with the concerns for an increased risk of fetal harm. Although a fetus can be harmed by radiation (including miscarriage, fetal anomalies, fetal growth restriction, intellectual disability, and future childhood cancer), the risk is low, especially at lower radiation doses. During the first 2 weeks of pregnancy, ionizing radiation is associated with an all-or-none type effect (miscarriage or intact survival) based on the radiation dose. After this time period, a dose less than 5 rads is recommended in order to decrease the chances of fetal harm.(9) A normal CT scan of the abdomen and pelvis delivers approximately 1 rad of radiation. As a rule, the least amount of ionizing radiation in necessary diagnostic tests should be utilized in the pregnant patient, and consultation with a radiologist and obstetrician is often helpful to achieve this goal.(9) A full discussion of the fetal risks

associated with CT scanning is beyond the scope of this commentary, but a CT scan in this setting should only be obtained after obstetrical consultation.

In this case, at the first visit to the ED, the combination of abdominal pain, nausea, and vomiting appropriately raised concern for a nonpregnancy-related cause and triggered further investigations. The patient was found to have a leukocytosis and a positive urinalysis and was treated for urinary tract infection (UTI). At that first visit, she also should have had a urine pregnancy test and an ultrasound to establish the location and gestational age of the pregnancy. In addition, it would have been reasonable for the providers to have considered imaging, since the symptom constellation—5 days of constant abdominal pain, nausea, vomiting, abdominal tenderness on exam, and an elevated white blood cell count—were incompletely explained by a simple UTI. An ultrasound was performed when the patient returned to the ED and indicated a normal viable pregnancy. However, no further imaging was pursued. Given the severity and persistence of her symptoms despite treatment, a complete abdominal ultrasound (looking for nonpregnancy-related intra-abdominal pathology) would have been appropriate.

Case & Commentary—Part 2

The patient again returned to the ED within 24 hours with persistent complaints. She now appeared more ill, with increased abdominal pain on examination. Magnetic resonance imaging of the abdomen was performed and revealed a ruptured appendix with signs of peritoneal inflammation. The patient was taken immediately to the operating room and was found to have diffuse peritonitis secondary to the ruptured appendix. An emergent laparoscopic appendectomy was performed, which the patient tolerated well. Unfortunately, 3 hours after the operation, she had a spontaneous abortion and subsequent severe bleeding requiring multiple transfusions. She was discharged home days later.

In retrospect, it may not have been appropriate to discharge this patient from the ED after her initial presentation without further evaluation, and she experienced a tragic adverse event.

In early pregnancy, the symptoms of appendicitis are identical to those seen in the nonpregnant state: periumbilical pain that migrates to the right lower quadrant, accompanied by anorexia, fever, nausea, and vomiting. With advancing gestational age and in parous women, the diagnosis may become more challenging, largely due to the laxity of the anterior abdominal wall.(10) As the uterus enlarges and fills the peritoneal cavity, a possible cephalad movement of the appendix into the upper quadrant (Figure) can confuse the clinical presentation. Patients may actually present with right upper quadrant pain. Moreover, as the distance between the peritoneum and the appendix increases, peritoneal signs may be masked. Lastly, accurate imaging of the appendix becomes more challenging. Uterine contractions, more common in later gestation, also decrease the ability to accurately elicit peritoneal signs and abdominal tenderness on physical examination. Notwithstanding these variations, clinicians should be aware that right lower quadrant pain remains the most common symptom of appendicitis in pregnant women.(10) Given that appendicitis is the most common cause of acute abdomen in pregnancy, a high index of suspicion is warranted to decrease maternal and fetal morbidity and mortality. In this case, the patient had a somewhat uncommon presentation, with no localization of the abdominal pain. However, the nausea and vomiting and persistent symptoms should have led the clinicians to consider the diagnosis of appendicitis early in the evaluation.

If appendicitis is suspected, diagnostic imaging can help rule in or rule out the diagnosis. Ultrasound is the test of choice in this setting—the diagnosis of appendicitis is made when a noncompressible, blind-ended tubular structure greater than 6 mm is visualized in the right lower quadrant. Unfortunately, the appendix cannot always be visualized with ultrasound, and ultrasound may be less accurate in the setting of a ruptured appendix or with advancing gestational age.(11) The American College of Radiology

suggests MRI as the second modality when evaluating for appendicitis in the pregnant patient. The diagnosis is made with visualization of a fluid filled appendix greater than 7 mm in diameter. MRI has high sensitivity and specificity for diagnosing appendicitis.(12) However, MRI technology and expertise are not always available, especially in smaller hospitals or off hours. When this is the case, CT with or without contrast should be used. CT is readily available in most centers, and it has high sensitivity and specificity for the diagnosis of appendicitis. The diagnosis is made by visualization of a fecalith, an enlarged nonfilling tubular structure, or right lower quadrant inflammation. The use of contrast typically enhances diagnostic accuracy with the potential increase in fetal harm (see above). The decision to use contrast should balance the potential fetal harm with the possible delay in diagnosis from nonvisualization of the appendix if contrast is not used. A delay can lead to rupture of the appendix and increase fetal mortality. The fetal loss rate increases from 3%–5% in nonruptured appendicitis to as high as 25% if the appendix ruptures.(13) Maternal morbidity is also higher in the setting of a ruptured appendix.

Institutions should develop an algorithm for optimal imaging of pregnant patients with an acute abdominal process, and this algorithm should be communicated to all the clinicians that care for pregnant patients. The algorithm should take into account best practices as well as the expertise and capability of the radiology team. The goal should be to minimize ionizing radiation and fetal harm while maintaining diagnostic accuracy. The use of the algorithm as well as the clinical outcomes of pregnant patients with abdominal pain should be audited and reviewed. The results of these reviews should be provided to clinicians and could easily be incorporated into institutional meetings that focus on hospital improvement.

The implementation of a checklist may also help to decrease morbidity in the pregnant patient who presents with abdominal pain without introducing any negative effect on safety. Checklists in medicine have been associated with reduced morbidity and mortality, enhanced communication, decreased adverse events, and improved adherence to hospital operating procedures.(14) A computerized checklist could review atypical signs and symptoms in the pregnant patient and prompt clinicians to consider other diagnoses. In this case for example, 5 days of abdominal pain, nausea, and vomiting, with abdominal tenderness on physical examination should have prompted an exploration of diagnoses other than a UTI and may have led to abdominal imaging.

In the above case, in the initial visit, pregnancy location and gestational age should have been documented, and a further investigation into the patient's signs and symptoms should have prompted imaging of the abdomen and pelvis and consultation with an obstetric specialist. When the patient returned with worsening symptoms, appropriate imaging was pursued and revealed acute appendicitis. The error (delay in diagnosis) led to a catastrophic adverse event—the loss of the fetus. A checklist highlighting the warning signs above or an algorithm for early and safe imaging may have led to an earlier diagnosis and a better outcome.

Baffled by Botulinum Toxin

The Case

A 5-year-old boy with a history of transverse myelitis with resultant spasticity of both lower extremities, gait abnormalities, neurogenic bladder, and neurogenic bowel presented to the rehabilitation medicine clinic for scheduled botulinum toxin (Botox) injections to his legs. He had been receiving Botox injections approximately every 3 months to his bilateral hamstrings, hip adductors, and gastrocnemius. Due to the patient's age and parent preference, he was given a dose of midazolam for sedation in the office prior to his injections.

The attending physician, fellow, and nurse went in the room to perform the injections. A time out was completed and the patient information, procedure, and sites were verified. About halfway through the 12

injections (2 to each muscle group on each side), the patient's mother said, "Wow, he is responding much better to the injections and sedating medications this time than he did 3 weeks ago." The attending and fellow were confused, as it had been 3 *months* since his last injections in the rehabilitation medicine clinic. Upon further questioning, the mother clarified that the clinicians in the urology clinic had had Botox injected 3 weeks earlier for management of the patient's neurogenic bladder. The scheduled injections were completed, followed by a long discussion held with the mother about the risk of antibody formation and decreased efficacy from too-frequent injections.

Despite the concerns, the patient had no adverse effects and experienced good results from the injections. However, after the procedure, the attending and fellow reviewed the electronic medical record (EMR) in an effort to understand how this error occurred. They realized that many specialties have begun to use Botox, and each one documented its use differently in the EMR. Whereas the rehabilitation medicine clinic entered a formal procedure note for each treatment, the urology clinic simply documented its injections in progress notes. Procedure notes appeared in a different area of the EMR and were not readily visible to clinicians accustomed to reviewing progress notes or test results.

Based on this review, clinic intake procedures were changed so that nurses now always ask about prior or recent Botox injections. In addition, the hospital's IT department created a clinical alert within the EMR that clearly states when the last order of Botox was given when a provider attempts to order Botox.

Breathe Easy: Safe Tracheostomy Management

The Case

A 75-year-old man was admitted to the hospital with sepsis due to multilobar pneumonia. He rapidly developed acute respiratory failure with evidence of acute respiratory distress syndrome that required mechanical ventilation. The patient improved with initial treatments but on hospital day 12, a decision was made to place a tracheostomy given the anticipated need for a prolonged respiratory recovery period. The patient reported feeling more comfortable after the tracheostomy than he felt with the endotracheal tube.

A few days later, the patient became increasingly agitated due to delirium. He developed acute hypoxia and respiratory distress when it was noted that his tracheostomy was dislodged. The critical care physician on call was notified and he tried to reinsert the tracheostomy tube. Multiple unsuccessful attempts were made and the patient ultimately went into cardiac arrest. The code team arrived and placed an endotracheal tube to secure the airway, which allowed successful resuscitation of the patient. The patient improved once again, had his tracheostomy replaced, and was eventually discharged to an acute rehabilitation facility for continued recovery.

Privacy or Safety?

The Case

A 64-year-old man with advanced dementia was admitted after being placed on a hold for grave disability. Family members noted he had a week of worsening confusion and agitation. The patient was undergoing a diagnostic workup for his altered mental status with a plan for a brain MRI if the etiology was still unclear. The cross-covering overnight resident was following up on the studies and placed an order for a brain MRI as discussed with the primary team at signout.

In this hospital, signout occurred with a paper-based system. In order to protect patient privacy, hospital policy dictated that signout documentation includes only patients' initials rather than more identifiable information such as full names or dates of birth. In this case, the patient requiring the brain MRI had the

same initials as another patient on the same unit who also happened to have severe cognitive impairment from a traumatic brain injury. The cross-covering resident mixed up the two patients and placed the MRI order in the wrong chart. Because the order for a "brain MRI to evaluate worsening cognitive function" could apply to either patient, neither the bedside nurse nor radiologist noticed the error. The following morning, the primary team caught the error and the MRI was canceled and ordered for the correct patient. The near miss led to several discussions about optimizing signout processes while also protecting patient privacy.

Unseen Perils of Urinary Catheters

The Case

A 68-year-old man with a history of hypothyroidism, hypertension, seizures, cerebral vascular attack with hemiplegia, dysphagia, vascular dementia, speech disorder, benign hypertrophy of prostate with urinary retention, and monocular blindness was admitted to the hospital. He had no known allergies. The patient required total care for his activities of daily living. He received bolus feedings through a gastrostomy tube and required occasional suctioning of his tracheostomy. He was incontinent of bowel and bladder. He was alert and oriented to person and place. He was only able to answer simple yes-or-no questions.

During the day-to-evening shift change, a nursing assistant reported the patient had not voided all shift. The patient's bladder was not distended nor did he complain of discomfort. The hospitalist was called and ordered a urinary catheter insertion. Just prior to insertion of the catheter by a registered nurse (RN), the patient voided but the amount was not recorded. The RN reported this to the charge nurse, who informed the RN to proceed with the catheter insertion. The RN did so, but the procedure did not produce any urine. Since the patient had just voided, the RN assumed the patient's bladder was empty. Two hours later, the patient began to complain of discomfort. The RN attempted to irrigate the catheter but met resistance.

The charge nurse was called to assess the situation and found a blood clot in the tubing. The hospitalist was notified and ordered continuous bladder irrigation (CBI). The same RN removed the catheter and inserted a three-way catheter and the CBI began. An hour later, the patient's pain increased and his bladder was distended. The CBI intake and output were in equal amounts. The patient was transferred to emergency room. A urologist was called, who performed a bladder scan and discovered the urinary catheter was not in the bladder. The second catheter was removed and a new three-way catheter was inserted by the emergency room RN. Blood returned from the new catheter. It was irrigated until clear, and then CBI resumed. The patient was transferred back to the ward for observation and the next day he received two units of blood. CBI was continued for 2 days.

The patient experienced pain from a distended bladder, a misplaced catheter, and three catheter [re-]insertions. He was put at risk for complications that included urinary tract infection, urosepsis, and bladder rupture. The misplaced catheter caused trauma to the urethra and blood loss. The patient's wife filed a complaint with the facility, which prompted an in-house investigation. The investigation revealed that the nursing staff on duty were unaware of the policy regarding bladder scanning prior to catheter insertion or the CBI policy that required documentation of both input/output and urinary volume.

Inflicting Confusion

The Case

A 26-year-old man with recently diagnosed Crohn disease presented to the emergency department with acute-onset abdominal pain, nausea, vomiting, anorexia, and an inability to pass gas. His white blood cell count was elevated and imaging revealed a small bowel obstruction and ileitis consistent with a Crohn flare. The patient was admitted to the medicine team, started on empiric antibiotics, and placed on bowel

rest. The medicine team recently managed a patient with Crohn disease and a similar presentation in which a gastroenterology (GI) consult recommended infliximab therapy. After they concluded that this flare was similar in its degree of acuity as the prior patient's, the medicine team preemptively initiated infliximab therapy and called for a GI consultation. GI recommended sending stool studies, including for *Clostridium difficile* infection (CDI), and suggested infliximab therapy should be initiated only after the stool studies were negative for infection. However, while an order was placed for stool studies, the primary team did not discontinue the infliximab. The next day, an hour into the infliximab infusion, a stool study returned and confirmed CDI. Infliximab was discontinued at that point, and the patient was treated for the CDI with eventual improvement in his symptoms.

Anchoring Bias With Critical Implications

The Case

A 61-year-old man with a history of stroke initially presented to his primary care physician (PCP) complaining of burning pain and numbness in his left foot for one month. The exam was notable for loss of sensation to his knee and a foot drop secondary to his prior stroke, but his pulses were intact with no other abnormalities noted. The PCP attributed the patient's pain and numbness to a peripheral neuropathy and referred him to podiatry.

The patient presented four more times to his PCP and twice to urgent care with a similar complaint of left foot pain. Each time he was referred to podiatry, but he never went to any podiatry appointments. During these visits, a complete extremity exam was not performed or documented, and the complaint was repeatedly attributed to his prior diagnosis of peripheral neuropathy.

After multiple visits to his PCP and urgent care over a 2-month period, the patient presented to the emergency department with worsening symptoms. On exam his left lower leg was dusky in color with extreme tenderness to palpation and his pulses could not be palpated. A computed tomography angiogram revealed complete occlusion of the left superficial femoral artery secondary to atherosclerotic peripheral arterial disease. The patient required emergent bypass surgery of the left leg by vascular surgery. Unfortunately, due to ischemia (lack of blood flow from the arterial disease) of his leg, he developed multiple infections postoperatively and ultimately required an above-the-knee amputation.

The vascular surgeons who cared for the patient believed the patient's chronic burning pain was likely due to progressive peripheral arterial disease and not to a peripheral neuropathy.

Departure From Central Line Ritual

The Case

A 55-year-old man with a history of poorly controlled diabetes mellitus, pancreatic insufficiency, and alcohol and cocaine abuse was found unconscious by his neighbors. The patient had last been seen 2 days prior and complained of dizziness, thirst, and nausea. Emergency medical services found him unresponsive, with a Glasgow Coma Scale score of 3. He was intubated in the field. Upon arrival in the emergency department (ED), his pH was less than 6.8, carbon dioxide 37 mm Hg, oxygen 80 mm Hg, potassium 7.8 mEq/L, glucose 1400 mg/dL, lactate 11.2 mg/dL, and anion gap 42 mEq/L.

A right internal jugular line was placed for access. The resident who placed the line was relatively experienced in line placement but was unable to confirm placement with ultrasound. Instead he used manometry, which was not a part of the normal ED routine for line placement. He ultimately chose to pull the line. Just then, another trauma patient arrived, and the supervising attending physician left the room.

The resident opened a second line insertion kit and restarted the process. Ultrasound was used to confirm correct placement. Upon flushing the line, it was noted that one of the ports was not working. The patient soon went into atrial tachycardia, which broke with adenosine. A chest radiograph was not obtained until later, after the patient went into ventricular fibrillation in the intensive care unit.

When the chest radiograph was finally completed, a retained wire was noted in the pulmonary artery. The interventional radiology team was consulted for wire removal. The retained wire likely caused a cardiac arrest, which required shocks, chest compressions, and cooling. After guidewire removal, the patient had no further episodes of arrhythmias, but experienced several other serious complications during a prolonged and stormy hospitalization.

Transitions in Adolescent Medicine
The Case

A 21-year-old woman with a history of Marfan syndrome complicated by aortic root dilation presented to the emergency department with abdominal pain and was found to be pregnant. This was her second pregnancy, as she had had a therapeutic abortion 4 years previously. At that time, the patient was being followed by a pediatrician and a pediatric cardiologist. They had advised her of the high-risk nature of the pregnancy, including a 10% chance that she could have an aortic rupture during pregnancy. She decided to terminate the pregnancy and was advised that she should undergo surgical repair of her aortic root in the near future. Shortly thereafter, she turned 18 years old and was referred to an adult primary care physician and cardiologist for continued care. The patient never saw her new physicians and was never scheduled for the recommended cardiac surgery procedure. In fact, over the next 3 years she did not receive regular follow-up care at all, although she remained relatively healthy. She also never received pre-conception counseling or contraception, despite the risk to her health should she become pregnant.

Upon learning of the current pregnancy, the patient decided against another abortion. She was evaluated by adult cardiology and cardiac surgery, and she was advised to undergo an aortic root repair during her second trimester in order to minimize potential harm to the fetus while preserving her own health. Understandably, this decision caused significant anxiety for the patient and her family. She did undergo the procedure without complications and proceeded to have a healthy child at full term.

Errors in Sepsis Management
The Case

A 72-year-old woman with pulmonary hypertension, chronic obstructive pulmonary disease (COPD) on home oxygen, and coronary artery disease presented to the hospital with left-sided abdominal pain and shortness of breath. She had been hospitalized for an exacerbation of her COPD 3 weeks prior but had been doing well at home on home oxygen. In the emergency department, she was ill appearing and in some respiratory distress. Her vital signs were notable for a temperature of 38.6° C, heart rate of 115 beats per minute, blood pressure of 104/68 mm Hg, respiratory rate of 28 breaths per minute, and oxygen saturation of 86% on her baseline 2 liters. She was found to have decreased breath sounds at the left base and appeared dehydrated. She had a white blood cell count of 21.4 x 10^9/L, creatinine of 2.1 mg/dL (up from a baseline of 1.3 mg/dL), a lactate of 3.9 mmol/L, and an international normalized ratio (INR) of 1.5. A chest radiograph revealed an infiltrate in the left lower lobe and she was diagnosed with pneumonia.

The patient was given 1 liter of normal saline in the emergency department. However, because of her history of pulmonary hypertension and coronary artery disease, she was not given any additional

intravenous fluids. Blood cultures were drawn, and she received levofloxacin (administered approximately 3 hours after presentation).

She was admitted to the transitional care unit but slowly worsened. Twenty-four hours after admission, her blood cultures were growing methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin was added to her antibiotic regimen. Despite the antibiotics and additional intravenous fluids, she continued to deteriorate. The patient developed respiratory failure requiring mechanical ventilation as well as septic shock requiring vasopressors. Her illness progressed and in discussions with her family, the decision was made to withdraw life-sustaining therapies and allow her to die peacefully. She died on hospital day 4 with her family at her bedside.

Fire in the Hole!—An OR Fire

The Case

A patient was taken to the operating room (OR) to undergo a planned laparoscopic subtotal colon resection for a biopsy-proven adenocarcinoma. After resecting the segment of the colon where the tumor was located, the surgeon realized that he had accidentally lacerated the bladder. The laceration was located and sutured without difficulty, and the decision was made to irrigate the bladder to ensure its wall was intact. As the surgeons went about the task of bowel re-anastomosis (reconnection) in the darkened laparoscopic suite, the nurses set up the bladder irrigation equipment and began to flush the bladder with warm saline. None of the OR staff noticed that in the course of setting up the irrigation equipment, the circulating nurse had hung the large 3-liter bag of irrigating solution from the handle of the anesthesiologists' accessory "slave" monitor, directly above the major transformer that powers the device. As the procedure continued, the bag of saline began to drip directly into the power inverter. Suddenly, sparks and flames began shooting from the monitor tower, and the OR quickly filled with black smoke.

At this hospital, the OR staff conducted daily safety huddles and held timeouts before every procedure, both of which included physical verification and verbalization of fire safety measures available. In this case, the preoperative timeout included all members of the operating team agreeing on the current procedure's fire risk and the nurse verifying and verbalizing the location of the nearest fire extinguisher next to the OR door. The OR team immediately put this training into action. The anesthesiologist quickly shut down the purified oxygen, while the surgical team attempted to halt the procedure before they lost all visualization. The scrub nurse activated the overhead lights, grabbed the fire extinguisher near the room entrance, and was able to quickly put out the fire. Once it was extinguished and the monitor setup examined, the culprit was identified: the leaking bag of saline into the active transformer. Fortunately, neither the patient nor any member of the operating staff was injured as a result of this incident. The damaged equipment was promptly replaced and the procedure concluded without further incident.

Transition to Nowhere

The Case

A 75-year-old man with a history of prostate cancer, poorly controlled myotonic dystrophy, hypertension, and chronic kidney disease was admitted to the hospital with anuric acute kidney injury in the setting of angiotensin receptor blocker overdose. The patient initially required intensive care unit admission for urgent hemodialysis before having a return of renal function to his previous baseline. Discharge planning efforts created a series of challenges.

The patient was new to this health system (having recently moved to the area), had no primary care provider established yet, and needed close follow-up care. The inpatient team desired a 1-week follow-up

appointment to check renal function, potentially re-start medications held during hospitalization because of the renal failure, and ensure entry into the primary and specialty care systems. The next available primary care appointment was in 6 weeks, and the urgent care clinic only offered same-day appointments, leaving no way to schedule a visit there prior to discharge. The patient was instructed to call the urgent care clinic in 1 week for a same-day appointment. However, he never made it to the clinic. Nearly 2 weeks later, he presented to the emergency department with poorly controlled hypertension. Once his renal function was assessed and found to be back to baseline, his previously held antihypertensives were re-started, and he was sent home once again with the original primary care appointment now only a few weeks away.

Dissecting the Presentation

The Case

A 78-year-old woman with a past medical history of hypertension was in good health until she experienced acute onset of confusion, which resolved after a few minutes. Then she had two episodes of black and "tarry" foul-smelling diarrhea (i.e., melena, usually indicative of gastrointestinal bleeding). She was concerned about the symptoms so presented to the hospital. On presentation, she had no abdominal pain, chest pain, shortness of breath, or focal weakness in her arms or legs.

Her physical examination was notable for tachycardia. Her mental status examination was normal. Laboratory tests showed mild anemia and new acute renal insufficiency. Chest radiograph revealed some right hilar fullness but was otherwise negative, and electrocardiogram showed sinus tachycardia.

The patient was diagnosed with a transient ischemic attack and possible gastrointestinal bleeding, and she was admitted to a telemetry unit for monitoring and ongoing testing. She generally did well with no further confusion and resolving diarrhea. She did have a persistent sinus tachycardia.

On the morning of hospital day 2, she was found unconscious by the nursing staff and found to be in cardiac arrest; her cardiac rhythm was pulseless electrical activity. Despite maximal resuscitation efforts, the patient died.

Autopsy revealed the cause of death to be an acute aortic dissection (tear in the aorta) extending from the ascending aorta to the renal arteries, along with an acute hemothorax (blood in the chest cavity). The dissection was probably present on admission and the tear in the aorta had impaired blood flow leading to all of her symptoms, including the transient ischemic attack, the gastrointestinal bleeding, and the renal failure. The dissection likely worsened while the patient was hospitalized, and its rupture into her chest cavity was the terminal event.

Medication Mix-Up: From Bad to Worse

The Case

A 69-year-old man with chronic kidney disease and essential hypertension was admitted to the hospital with chest pain, headache, and accelerated hypertension. Of note, he had missed taking several days of his regular medications. Upon admission, his blood pressure was 218/126 mm Hg with a heart rate of 90 beats per minute. Physical examination revealed a patient in mild discomfort, but no distress, presence of an S4 (indicating reduced ventricular wall compliance), and otherwise normal cardiopulmonary and neurologic examination. His electrocardiograph revealed significant left ventricular hypertrophy but no acute ischemic changes. His chest radiograph demonstrated a mildly enlarged heart, but no widened mediastinum or pulmonary edema. Troponin levels were negative, and his kidney function tests were stable. After starting a nitroglycerin drip, it was decided his outpatient medications should be re-started

gradually. One of his antihypertensive medications was minoxidil, and his outpatient dose of 7.5 mg per day was ordered via the electronic health record. However, midodrine 2.5 mg tablets x 3, not minoxidil 2.5 mg tablets x 3 ultimately arrived on the medical unit.

While the medication mix-up was not identified by the dispensing pharmacist, the nurse responsible for administering medications noticed that the dispensed medication differed from what had been ordered. She sought out the medical team, who quickly clarified that the intended medication was minoxidil, not midodrine. Midodrine hydrochloride is a vasopressor/antihypotensive agent used in treating orthostatic hypotension. Had this patient received midodrine in the setting of accelerated hypertension and chest pain, his condition could have worsened significantly due to this pharmacological effect.

Critical Opportunity Lost

The Case

A 55-year-old woman presented to the emergency department (ED) with new onset chest pain. She reported eating a heavy dinner the previous night in celebration of her anniversary. She initially attributed her chest pain to acid reflux, but when the pain persisted, she arrived at the ED for further evaluation. During her ED visit, her symptoms resolved with sublingual nitroglycerine and a "GI cocktail" (an oral antacid/anesthetic combination sometimes used to treat possible reflux), and her electrocardiogram was unremarkable. She felt back to "normal" so the clinicians caring for her in an observation unit arranged for a stress test the following morning.

When the patient arrived for her stress test, she reported feeling well with no further chest pain. Approximately 3 minutes into her stress test, she collapsed and went into cardiac arrest. Resuscitation attempts were unsuccessful. The case was reviewed by the hospital's quality committee, whose members noted that the providers in the observation unit failed to note an elevated troponin prior to discharge. The facility recently transitioned to a new electronic health record and questions were raised about how critical or panic lab values should be managed. Providers felt that a lack of such a system had contributed to the error in this patient's care.

Two Wrongs Don't Make a Right (Kidney)

The Case

A 53-year-old man presented to Hospital A with abdominal pain and hematuria. Computed tomography (CT) imaging revealed a suspected renal cell carcinoma in the right kidney. He was transferred to Hospital B for surgical management.

All of the medical records from Hospital A documented a left-sided tumor—the wrong side. The CT scan from Hospital A was not available at the time of the transfer and repeat imaging was not obtained by the providers at Hospital B.

At the time of surgery, the surgeon was asked if the absence of an available image should preclude progressing with the surgery. He decided to proceed and, based on the available information, removed the left kidney.

The day following the surgery, the pathologist contacted the surgeon to report no evidence of cancer. The surgeon then reviewed the initial CT scan and realized his mistake. The patient underwent a second surgical procedure to remove the right kidney (which was found to have renal cell carcinoma). Having lost both kidneys, the patient was then dependent on dialysis, and because of the cancer, he was not a candidate for kidney transplant.

Haste Makes Care Unsafe

The Case

An 80-year-old man with a history of coronary artery disease and atrial fibrillation underwent a combined elective coronary artery bypass graft (CABG) and Maze procedure (ablation of atrial fibrillation). A pulmonary artery (PA) catheter was placed after induction of anesthesia in order to closely monitor the patient's hemodynamic status. The surgery was proceeding uneventfully when the surgeon requested that the PA catheter be pulled back from the pulmonary artery into the right ventricle when he performed the actual ablation. At that point, the surgeon was informed that another patient in the cardiac intensive care unit (ICU) would require an emergency CABG. The surgeon was the only cardiac surgeon available that day, and there was also only one cardiac anesthesia team. The surgeon and attending anesthesiologist decided to begin the emergency CABG as soon as possible after completing the current procedure.

The remainder of the CABG was completed without incident, and the patient was weaned off cardiopulmonary bypass (CPB) easily, but this process took nearly another hour. By this point, the second patient was already being brought to another operating room (OR), and the team had received several pages about his clinical status. The surgeon was anxious to start the second case as soon as possible, so in order to speed up the transfer process, the attending anesthesiologist refloated the PA catheter himself back into the pulmonary artery, which required re-inflating the catheter's balloon. As soon as this was completed, the anesthesiologist rushed to the other OR in order to begin the emergency CABG. An anesthesia resident accompanied the first patient to the ICU.

In the ICU, the nurse who assumed care of the patient noticed that the PA catheter waveform was dampened (the tracing was flat and did not vary with the cardiac cycle). Further check by him and the anesthesia resident revealed that the PA catheter balloon was still inflated, and probably had been so the entire time after refloating. This was potentially very dangerous, as leaving the balloon inflated could have caused catastrophic damage to the pulmonary artery. Fortunately, the nurse recognized the situation quickly, and the resident deflated the balloon and withdrew the PA catheter without the patient experiencing any harm. The anesthesia resident realized that she had not discussed the PA catheter explicitly (including its inflation status) with the attending prior to transferring the patient out of the OR.

Bowel Injury After Laparoscopic Surgery

The Case

A 30-year-old man presented to the hospital for a scheduled laparoscopic inguinal hernia repair with mesh placement. The patient had no significant past medical history and did not take any home medications. He was expected to stay a few hours after the surgery and then be released the same day.

The surgery went uneventfully, but after surgery, the patient continued to have high levels of pain at the surgical site. He was then admitted to the hospital for monitoring and pain control. As the team that performed the surgery had already left for the day, a resident physician who was unfamiliar with the patient provided overnight coverage. The night resident was called to the patient's bedside multiple times overnight by the charge nurse to address the patient's pain, and the resident ordered additional intravenous pain medication. When the primary surgical team arrived in the morning, they increased the patient's standing pain medication regimen and he was expected to be released that day or the next at the latest.

The patient remained in sustained pain and the surgical team was called to the bedside multiple times over the next 2 days. His physical examination was documented as unremarkable, and he was started on a patient-controlled analgesia (PCA) pump with hydromorphone. On postoperative day 2, the patient was weaned off the PCA and started on a clear liquid diet. However, the next day, he continued to have

abdominal pain and became increasingly tachycardic with slight abdominal distention and a low-grade fever. A computed tomography scan of the abdomen was ordered, and the patient was found to have a bowel perforation. He was sent urgently back into the operating room in order to fix the perforation, and postoperatively required a lengthy stay in the intensive care unit due to septicemia. He did eventually recover and was discharged home.

Monitoring Fetal Health

The Case

A 29-year-old woman had an uncomplicated pregnancy with a healthy fetus and presented to the hospital at term (40 weeks) in early labor. She progressed slowly over the first night. By the next morning, she had a completely dilated cervix and was ready to push. She pushed for approximately 2 hours without any difficulty or any sign of problems with the fetus. Unfortunately, when the infant was born, he was cyanotic and flaccid with very low Apgar scores. An arterial blood gas at the time showed a pH of 6.70 (normal: 7.25–7.35), a profound acidosis. The infant required extensive resuscitation but survived and was transferred to the neonatal intensive care unit.

The infant subsequently had multiple seizures typical of hypoxic-ischemic encephalopathy (brain injury from inadequate oxygenation of the brain that occurred during childbirth) and other problems related to the complicated delivery. He spent a month in the neonatal intensive care unit before being transferred to a neuro-rehabilitation unit. He is likely to be severely disabled for the remainder of his life.

A root cause analysis of the case found that the mother had been appropriately monitored and had not shown any evidence of distress. The fetus had been monitored using the standard fetal heart rate tracings throughout the time of labor. The fetal heart rate tracings had shown evidence of Category 2 and 3 abnormalities (moderate-to-severe fetal distress) for at least 90 minutes prior to the delivery. These abnormalities, which likely would have prompted an urgent cesarean delivery, had not been recognized by any of the physicians or nursing staff.

In this institution, continuous fetal heart monitoring of all of the women in labor was displayed centrally on a large 40-inch monitor at the nurses' station. On this screen, the individual fetal heart monitoring strips for the 16 rooms were displayed continuously in small windows. Two nurses at the nursing station were assigned to watch the monitor at the time of the concerning abnormalities. When asked about the incident, they both replied that they "just didn't see the bad tracings" and commented how difficult it can be sometimes to identify abnormalities and to continuously watch all 16 small windows. The responsible obstetrician was busy throughout the period of abnormal tracings with another complicated childbirth.

Medical Devices in the "Wild"

The Case

A 75-year-old man with a history of congestive heart failure (CHF), coronary artery disease, diabetes, chronic pain, arthritis, and hyperlipidemia was admitted to the hospital with a CHF exacerbation manifesting as lower extremity edema and weight gain. At baseline, he was able to function independently and perform all activities of daily living. The patient was treated with diuretics, fluid restriction, and was given dietary and medication education. After a short period of treatment, his swelling improved and he was able to ambulate on the hospital ward without difficulty. The medical team was preparing the patient for discharge the following day.

That afternoon, the patient was lying in bed watching television when his nurse came into the room to assess him. The bed was low to the ground and locked in position, so she raised the bed up to perform her

assessment. The patient had sequential compression devices (SCDs) in place to prevent deep venous thrombosis (DVT). When the nurse raised the bed, unbeknownst to her, the tubing for the SCDs caught on the bed wheel lock and unlocked the bed. After completing her assessment, the nurse left the room. Having been told he should ambulate several times daily, the patient then sat up on the side of the bed and attempted to stand. In doing so, he pushed down on the bed with his hands. When he did this, the bed rolled out from under him and he fell onto his left side. He immediately complained of hip pain, and on radiographs was found to have a broken left hip.

The next day he went to surgery for planned open reduction and internal fixation of his hip fracture. Unfortunately, he developed respiratory issues and had to be transferred to the medical intensive care unit for closer monitoring postoperatively. He did improve temporarily, but despite receiving appropriate DVT prophylaxis, one week after surgery he suddenly experienced a cardiac arrest and was found to have a massive pulmonary embolism. He was briefly resuscitated but died a short time later.

The unit where the fall occurred called a multidisciplinary "fall huddle" to reenact the circumstances of the incident. The nurse was certain the bed was locked, but a technician noticed that the SCD tubing had fallen around the wheel and brake of the bed. During the reenactment, the staff realized it was possible for the tubing to catch the brake and unlock the bed without being noticed. The hospital's patient safety department immediately informed the company that manufactured the beds and the SCD equipment. The SCDs were replaced with newer equipment that had shorter tubing that could not wrap around the bed brake and unlock it inadvertently.

Ebola: Are We Ready?
The Case

A 28-year-old man, well-appearing but pale, walked into the emergency department (ED) on a Wednesday afternoon at 3 PM complaining of nausea, vomiting, and fever since morning. The patient stated that he was at a potluck the night before and thought he ate something that made him sick because he had a foul tasting potato salad. He was unsure if anyone else got sick. The patient glanced at the sign prominently posted at the triage desk. "Tell us if you have traveled outside the United States in the past month." He did not volunteer any information, but when the triage nurse asked him directly, he reported that he returned the previous week from Sierra Leone, where he was volunteering with Doctors Without Borders handling patient intake. Because of this history, the nurse initiated an isolation protocol for patients with symptoms and travel history consistent with possible exposure to Ebola. The triage nurse donned a mask and handed one to the patient, asking him to don it as well. She did not touch him but asked him to go with her to a decontamination room and to wait there until staff could don personal protective equipment (PPE). The patient was also instructed to don a blue plastic gown over his street clothes. He waited in the decontamination room for 20 minutes.

An ED physician and nurse, both wearing full PPE, introduced themselves to the patient and explained why they were dressed in coveralls, powered air purifying respirators, double gloves, and protective leg and shoe covers. They took a history and assisted the patient to a gurney. Outside the room, two security officers cleared the corridor. The physician and nurse pushed the gurney down the secured hallway toward the elevators where they would go up to an isolation room. There seemed to be confusion as to which elevators should be used. At that moment three different elevators arrived on the ground floor, more than 30 staff members (at their shift change) exited the elevators to go home and were surprised to see the two human silhouettes covered head-to-toe in yellow and white spacesuits pushing a gurney occupied by a pale young man, now garbed in an isolation gown, bonnet, and mask, and in considerable distress with vomiting. As the patient arrived in the isolation room, the ED nurse was asked to start an IV, draw blood, and insert a Foley catheter. As the nurse gathered supplies and cannulated the peripheral

vein, she asked, "Where is the transfer set?" referring to an equipment tray used in the ED to draw blood from a peripheral IV. As the clinicians soon discovered, this set was not available on the patient unit. The blood was successfully collected using available equipment, yet the procedure to send it to the laboratory was not clear. The specimen was placed in a double biohazard bag and left in the room pending additional instructions about how to transport it to the laboratory.

The critical care team, two intensivists and two nurses, arrived in the isolation room. A trained observer assisted the critical care team as they donned their PPE, a process that took more than 20 minutes. A warm handoff was provided by the ED team as they exited. A warm handoff includes an in-person summary of the patient's history, symptoms, and ED care and decision-making, with an opportunity for the critical care team to ask questions. As the critical care team turned to the patient, he vomited again, became tachycardic and hypotensive, and his oxygen saturation dropped and did not respond to supplemental oxygen. The intensive care unit (ICU) physicians decided the patient needed central venous access and requested supplies and ultrasound. While they often supervise resident and fellow insertions of central lines, attending physicians in the ICU seldom perform insertion themselves. Unfamiliar with the central line kit, they struggled but successfully put a triple-lumen catheter in the internal jugular vein using ultrasound guidance. Sterile technique was breached multiple times as they navigated the central line insertion process in their bulky PPE. At several points in the process as they reached for supplies, their backs were to the patient. An airway was never secured.

Fortunately, this case was only a simulation. Multiple experts observed and provided feedback on the process.

Although the patient was not harmed, he was placed at risk for development of a central line–associated bloodstream infection. Hospital faculty and staff were placed at risk of contamination with Ebola. Yet, this simulation took place in a hospital that was "ready" for a patient with Ebola. The hospital had developed and disseminated guidelines for caregivers and had trained them especially on safe PPE donning and doffing.

A Stroke of Error
Case & Commentary—Part 1

A 67-year-old man with a history of untreated hypertension presented to the emergency department (ED) after a fall. On presentation, he was noted to have a systolic blood pressure of 220 mm Hg and word-finding difficulties of unclear duration. Laboratory results were notable for an elevated troponin of 0.2 µg/L and an elevated creatinine of 1.9 mg/dL (but there was no baseline comparison for the latter). To further evaluate his neurologic deficit, the ED obtained a CT scan of his brain without contrast before admitting him to the cardiology service with a working diagnosis of hypertensive emergency. The head CT demonstrated extensive white matter hypoattenuation, which was greater than expected for his age, but no focal findings. The cardiology team ordered an MRI to further characterize these findings, but the patient was unable to tolerate it due to his altered mental status. Neurology was not formally consulted.

The initial neurologic evaluation of a patient with suspected stroke necessitates a rapid and focused assessment. The history should center on establishing the time of symptom onset or the time the patient was last known to be neurologically normal if the time of symptom onset cannot be confidently established. The interval between symptom onset and clinical assessment will determine whether acute reperfusion therapy for ischemic stroke can be considered. The neurologic examination should focus on identifying signs of lateralized hemispheric or brainstem dysfunction consistent with stroke. The National Institutes of Health Stroke Scale (NIHSS) is a validated 15-item scale (Table) that assesses key components of the standard neurologic examination (1) and has been widely adopted into routine clinical

practice. Brain imaging is the only reliable means to differentiate between ischemic and hemorrhagic stroke.(2,3) Non-contrast head computed tomography (CT) is the imaging modality most readily available in most stroke centers. CT is sensitive to intracranial hemorrhage and may be rapidly performed as part of the acute stroke evaluation.

Blood pressure is commonly elevated in patients with acute stroke and may be related to the stress of cerebral infarction, pre-existing hypertension, or a response to increased intracranial pressure.(4) Arterial blood pressure spontaneously declines in most patients with ischemic stroke within the first 24 hours of admission.(5) Extreme elevations of blood pressure can result in end-organ damage manifesting as cerebral, cardiac, or renal dysfunction. In this case, the elevated serum troponin and creatinine may have indicated cardiac and renal involvement secondary to uncontrolled systolic blood pressure. Disturbances of cerebral function due to hypertension typically result in diffuse symptoms that may include headache, change in mental status, or seizures. Focal symptoms are less common. In the acute setting, it may be difficult to differentiate between blood pressure elevation as the primary cause of end-organ dysfunction or as a secondary consequence of stroke. Framing effects, anchoring, and overreliance on test results are potential sources of diagnostic error.(6)

Neurological consultation in the emergency department can be considered when signs or symptoms of central or peripheral nervous system dysfunction are evident. Many common neurological presentations, such as migraine headache, can be reliably diagnosed and effectively treated by emergency department providers without neurological consultation. Patients with transient or persistent symptoms suggestive of hemispheric, brainstem, cerebellar, or retinal dysfunction warrant neurological consultation. In this case, the presentation was sufficiently complex to warrant neurological consultation in the emergency department. Detailed neurological examination by an experienced neurologist may identify subtle localizing signs suggestive of a vascular event and reduce the risk of missing an opportunity to offer acute reperfusion therapy to a potentially eligible patient. In hospitals without timely access to on-site neurological expertise, telemedicine has been leveraged to provide remote teleneurological evaluation.(7)

No BP During NIBP

The Case

An otherwise healthy 49-year-old man with atrial fibrillation was scheduled for ablation in the catheterization laboratory under general endotracheal anesthesia. The procedure lasted 7 hours. Per American Society of Anesthesiologists guidelines, monitoring included continuous electrocardiography, oxygen saturation, end tidal carbon dioxide, as well as noninvasive blood pressure (NIBP) measurement every 5 minutes. The patient was extremely stable with values hardly changing over time. Inadvertently between 4 PM and 5 PM, the NIBP stopped "cycling," but this was not recognized. When the attending anesthesiologist took over the case at the end of the certified registered nurse anesthetist's (CRNA) shift, she noticed that the "graphic trends" tab on the monitor had a straight line for heart rate and oxygen saturation (indicating no change over time) and a blank space for the NIBP. A lookup of numerical trend was done and it showed that the last NIBP recording was more than 60 minutes earlier. After discovering the error, the case continued without any problem. The patient was extubated and discharged home the next day as planned. The patient was informed about the mistake and he accepted it as human error.

Reviewing the case revealed that certain safety checks that are routine in the operating room (OR) do not routinely occur in the cardiac catheterization laboratory setting in this hospital. First, OR attending physicians are expected to frequently check the progress of the case. Second, the automated anesthesia

record in the OR shows "blank" if there are no new NIBP recordings. Third, the OR doctors' work area has a central monitor feed that the attendings watch when they do paperwork. Fourth, the OR monitors "gray" out NIBP value if the cuff is not cycling. These features are not in place for out-of-OR cases. In addition, the monitor for the catheterization laboratory was a different make and model from those in the OR, and the CRNA was unfamiliar with the menu and knobs. The anesthesia record was manual, and the CRNA kept documenting the same reading for a whole hour. Human factors such as fatigue and lack of vigilance in a very stable case also contributed to the error.

Too Much, Too Fast

The Case

A 68-year-old man with amyotrophic lateral sclerosis (ALS) was admitted to the intensive care unit (ICU) for fever, tachycardia, and increased respiratory secretions. His ALS was complicated by ventilator-dependence requiring a tracheostomy, along with comorbidities that included coronary artery disease and a prior bypass graft, insulin-dependent diabetes, hypertension, and hyperlipidemia. Initial physical examination and laboratory studies were suggestive of pneumonia with sepsis and poorly controlled hyperglycemia. His electrolytes were notable for sodium of 150 mEq/L, potassium of 3.7 mEq/L, and glucose of 421 mg/dL. He was treated with broad-spectrum antibiotics and fluid resuscitation while also being placed on an insulin infusion for his hyperglycemia.

Over the first few hours of hospitalization, his hemodynamics and glycemic control markedly improved. A repeat potassium level returned low at 2.7 mEq/L. Providers ordered 120 mEq of oral potassium replacement via a feeding tube and 60 mEq of intravenous potassium via a central line at 20 mEq/hour. While on the third bag of the potassium infusion, the patient went into cardiac arrest and advanced cardiovascular life support measures were delivered. Point-of-care testing showed potassium was critically elevated at greater than 9.0 mEq/L. Despite efforts to aggressively treat the hyperkalemia, resuscitation attempts were unsuccessfu

A Lot of Pain (Medications)

Case & Commentary—Part 1

A 58-year-old man was admitted to the hospital with a non-healing foot ulcer related to severe peripheral vascular disease. He also had a history of chronic obstructive disease and chronic pain. His pain was long-standing and related to multiple prior neck and back surgeries. For years he had been treated with long-acting morphine (extended-release 40 mg twice daily) as well as additional opioids for breakthrough pain. On admission, he reported 8/10 pain, despite receiving his home opioid regimen. After a surgical amputation to treat the ulcer, his pain worsened to 10/10.

Rates of opioid use, and long-term use for chronic non-cancer pain, have markedly increased over the last 2–3 decades.(1,2) Although data regarding the prevalence of chronic opioid use in hospitalized patients are sparse, one recent study found that more than 25% of patients hospitalized at Veterans Administration Hospitals were receiving chronic opioid therapy, defined as 90 days or more of opioids prescribed in the 6 months prior to hospitalization.(3) Furthermore, patients receiving chronic opioid therapy consume a disproportionate share of health care resources, including significantly more emergency room visits and days in the hospital.(4) The issue faced by providers caring for the patient in the case, therefore, is quite common: How should management of acute pain in hospitalized patients receiving chronic opioid therapy be approached? Embedded in this question are issues relating to efficacy and safety; specifically, finding the right balance between achieving adequate analgesia and avoiding adverse effects or problems with opioid misuse and/or addiction.

Achieving adequate analgesia in patients on chronic opioid therapy is challenging. There are well-described pharmacodynamic issues that make pain control more difficult to achieve in patients on chronic opioids, including tolerance (higher doses of opioids are required to maintain the same level of analgesia) and opioid-induced hyperalgesia (patients experience greater pain with less noxious stimuli). Thus, not only are patients on chronic opioids more likely to be hospitalized, but they may be more likely to experience acute pain while in the hospital. Physicians, on the other hand, may be reluctant to provide additional opioids due to concerns over adverse effects, particularly while prescribing the higher doses often required in this patient population. Physicians and other providers may also have concerns about abuse or contributing to addiction. All of these factors can result in under-treatment of pain in this patient population.(5)

When evaluating a patient on chronic opioids for acute pain, a thorough understanding of the nature or quality of the pain and its relationship to the patient's chronic pain complaint is crucial. We are told that the patient in this case experienced a "worsening" of his pain after his surgery, but it is not clear whether this was worsening of his chronic neck and back pain or worsening of his foot pain. This information would be essential in assessing response to therapy. Opioid escalation for acute foot pain in the setting of a surgical amputation should be identified as such, and opioid requirements should be expected to gradually decrease with passage of time after the operation. Lack of improvement with time could indicate a post-operative complication, tolerance, or possible addiction. Additionally, a better understanding of the nature or quality of the pain could assist in identifying the optimal treatment strategy. For example, inflammatory pain is optimally treated with nonsteroidal anti-inflammatory drugs (NSAIDs), while neuropathic pain may respond well to the addition of gabapentin or pregabalin, or consultation with a pain management specialist for consideration of a nerve block.(6) These non-opioid medications, when combined with opioids, have been demonstrated to improve pain control and lower opioid requirements in the acute care setting.(6) Accordingly, the American Society of Anesthesiologists recommends a multimodal approach to pain management, using at least two different classes of analgesics.(6)

Once a decision has been made to use opioid analgesics to manage acute post-operative pain, identifying the optimal drug, dose, route, and regimen are important in assuring a favorable risk-to-benefit ratio. Guidance on these decisions comes mostly from expert opinion.(6,7) The patient's previous long-acting opioid should be continued, if possible, to deliver the patient's usual baseline analgesia and avoid precipitating withdrawal. When adding additional opioids for acute pain, immediate-release opioids should be used to facilitate dose titration. The oral route of administration is preferred when possible to maximize duration of action and reduce addiction potential. If pain is severe and immediate control is necessary, intravenous opioids may be initially required, and consideration should be given to patient-controlled analgesia in an alert patient. If possible, the immediate-release opioid chosen for management of acute pain should be the same type as that used for chronic pain, to minimize chances of side effects and adverse effects due to incomplete cross-tolerance and facilitate ease of dose calculations. The patient's total daily opioid consumption prior to hospitalization should be ascertained as accurately as possible and converted to a baseline daily oral morphine equivalent—several online or handheld device calculators are available for this conversion. In general, an initial dose of 10%–20% of the baseline total daily dose should be used, with an as-needed frequency based on the estimated duration of action—approximately 4 hours for oral, and 3 hours for intravenous.(8,9)

In the event that adverse effects or other considerations necessitate changing to a different opioid than the chronic medication, guidelines advise starting with a dose 25%–50% lower than the calculated equianalgesic dose, to avoid unintentional overdose in the setting of incomplete cross-tolerance.(10) In selecting an alternate opioid, there are a few key considerations. Due to their metabolism, morphine and hydromorphone have fewer drug–drug interactions than other opioids.(11) However, most opioids,

including morphine and hydromorphone, are eliminated primarily in the urine, necessitating dosage adjustment in the presence of renal failure.(11)

With respect to the patient in the case, his outpatient dose of 40 mg extended-release morphine twice daily should be confirmed and continued. For his superimposed acute pain, since his primary outpatient opioid is morphine, immediate-release morphine would be an appropriate choice. The recommended dose would be 10%–20% of his baseline of 80 mg daily, which is 8–16 mg orally, every 4 hours as needed, with adjustment based on response. Given the inflammatory nature of his pain, an NSAID should be administered as well, assuming there is no contraindication.

Case & Commentary—Part 2

In addition to post-operative surgical pain and his chronic pain, he also began having diffuse severe muscle spasms. Over the next 48 hours he was given increasing doses of extended-release morphine (up to a dose of morphine 165 mg orally three times a day), as well as intravenous and oral hydromorphone for breakthrough pain. In the afternoon on post-operative day 3, he was found to be somnolent, with an oxygen saturation of 87% on room air. His other vital signs were unremarkable and his oxygen saturation improved to 92% on 2 liters of oxygen by nasal cannula. His afternoon dose of extended-release morphine was held by the primary nurse who notified the surgical resident on duty.

The patient did well until 3 hours after the dose had been held, when he became more alert but complained of 10/10 pain in his post-surgical leg and had tremors and diffuse muscle spasms. The nurse treated his symptoms with hydromorphone 6 mg orally and 1 mg intravenously per the prescribing orders.

The surgical resident was contacted to evaluate the patient and requested the extended-release morphine be given for the ongoing severe pain. The nurse, reluctant to administer this medication in light of the recent episode of somnolence, attempted to explain his reasoning for withholding it but the resident insisted on having him administer the medication. In addition, the patient was writhing in bed with muscle spasms so the resident prescribed diazepam 5 mg intravenously (a muscle relaxant the patient had not been previously prescribed).

Approximately 5 minutes after the diazepam was given, the patient turned pale and became minimally responsive. He was found to have a respiratory rate of 5 breaths per minute. A code blue was called for opioid and benzodiazepine overdose. Fortunately, the patient responded well to intravenous naloxone (an agent that acutely reverses the effects of opioids) and increased oxygen by non-rebreather mask.

He was transferred to the intensive care unit for ongoing monitoring and treatment with naloxone. He was found to have new acute renal insufficiency, which likely had contributed to a build-up of opioids, enhancing their effects. He recovered well and was transferred back to the surgical unit 3 days later. He was ultimately discharged without any long-term effects.

Opioids are among the top causes of drug-related adverse outcomes in hospitalized patients.(12) The most severe adverse event, opioid overdose, is difficult to estimate owing to varied definitions of this endpoint and varied patient populations; however, estimates range from 0.2%–4% of those exposed in the inpatient setting.(13-15) Predictors of opioid-related adverse events include *patient-related factors* such as age (15,16), obesity (15,16), renal or hepatic failure (11), sleep apnea (16), chronic obstructive pulmonary disease (16), and *prescribing-related factors*, such as high doses—particularly doses of more than 100 mg oral morphine equivalents per day (16,17) and co-prescription of other sedating medications.(17) Thus, the patient in this case had several factors associated with heightened risk of an opioid-related adverse

event, including opioid doses in excess of 100 mg daily, use of multiple opioid drugs with likely incomplete cross-tolerance, co-prescription of other sedating medications, and renal failure.

Studies demonstrate that among the phases of the medication-use process, the prescribing phase contributes most to confirmed opioid overdoses.(18) Improper monitoring is the second most common contributor.(18) This would suggest that multimodal initiatives (as opposed to a single simple solution) aimed at improving prescribing and monitoring practices may have the highest yield in preventing opioid-related overdose in the inpatient setting. However, limited guidance exists on the best methods for achieving these aims in the inpatient setting, and most recommendations are based on expert opinion rather than implementation studies.

In 2012, The Joint Commission issued recommendations for safe use of opioids in hospitals.(18) Although many of these recommendations are based solely on the opinion of experts in the field, they make intuitive sense and provide guidance where few data exist. With respect to improving *prescribing*, they recommend a combination of education, information technology, and oversight and consultation with pain management specialists. Education should include advising clinicians to use both pharmacologic and non-pharmacologic methods of pain management. In addition, clinicians should be educated on the use of non-narcotic analgesics either as first-line therapy or in combination with opioids. Information technology can be used to support desired prescribing practices, build alerts for unsafe prescribing, and provide conversion support to calculate correct doses of opioids. Institutions are encouraged to create policies and procedures that allow for second-level review and/or consultation by a pain management specialist or pharmacist when doing the following: (i) converting from one opioid to another, (ii) changing the route of administration (i.e., from oral to intravenous or transdermal), or (iii) using high-risk opioids such as methadone, fentanyl, and intravenous hydromorphone.(18) Beyond these recommendations, there are no additional guidelines regarding a threshold at which providers should consult a pain service or other expert. However, most would agree that uncertainty about opioid prescribing decisions, difficulty achieving adequate analgesia, suspected addiction, and managing opioids in a patient with risk factors for adverse events (see above) should all prompt consideration of consultation.

The Prescription Drug Monitoring Program (PDMP) is an additional resource that can improve opioid prescribing by assisting with outpatient opioid dose confirmation and identification of potential addiction, misuse, or diversion. PDMPs, presently available in 49 states, are state-run electronic databases used to track pharmacy dispensing of controlled substances to patients. Studies have demonstrated that PDMPs can influence prescribing in primary care and emergency department settings (19), and it seems logical that they would similarly improve prescribing practices in the inpatient setting. Hospitals should work toward linking PDMPs to electronic health records so that PDMP information is available at the point of care, as recommended by the Centers for Disease Control and Prevention.(20)

With respect to improving monitoring of patients receiving opioid medications in the inpatient setting, The Joint Commission recommends performing serial assessments of respiration and the depth of sedation, particularly when increasing the opioid dose or changing from one opioid to another.(18) However, the method and frequency of such assessments is not specified. They also suggest using continuous pulse oximetry to monitor oxygen saturation. It is important to keep in mind that oxygen saturation can be falsely normal in the setting of supplemental oxygen, and pulse oximetry, therefore, cannot be relied upon as the sole monitoring approach in this setting. Since continuous pulse oximetry is presently a limited resource at most hospitals, future research is necessary to determine which patients may benefit most from this monitoring strategy. In the absence of such data, consider continuous pulse oximetry when increasing the opioid dose, changing from one opioid to another, or in patients with risk factors for adverse events.

Although the patient described ultimately did well, the case illustrates many of the common errors in opioid prescribing for acute pain in a hospitalized patient on chronic opioids. A distinction should have been made between the patient's chronic pain, for which continuation of his usual dose of extended-release morphine would have been appropriate, and his acute postoperative pain, for which immediate-release opioids are more appropriate. Incomplete cross-tolerance to hydromorphone likely played a role, and using intravenous hydromorphone in addition to oral is not only unnecessary, but makes total dosage calculations more difficult, thereby increasing risk of overdose. Morphine and hydromorphone should be dose reduced in the setting of renal failure, and benzodiazepines should generally be avoided in patients on opioids. Consultation with a pain management specialist would likely have prevented these prescribing errors and the associated adverse outcome.

Take-Home Points

- Taking a thorough history regarding the nature of the pain, and differentiating acute from chronic pain, is crucial in directing optimal treatment and optimal monitoring of response.
- Always combine opioid and non-opioid analgesics to maximize analgesia and reduce opioid requirements. For acute pain, use immediate-release opioids to allow dose titration, preferably via the oral route, starting at a dose of approximately 10%–20% of the patient's total baseline opioid requirement. If changing to a different opioid, use a dose 25%–50% lower than the calculated equianalgesic dose.
- Most opioids, with the exception of fentanyl, need to be dose reduced in the setting of renal failure.
- Avoid co-prescription of other medications with sedating properties—particularly benzodiazepines.
- Consider consultation with a pain management specialist for patients at high risk of an opioid-related adverse event, or in situations of uncertainty or suspected addiction.
- Hospitals should work toward integrating Prescription Drug Monitoring Program information into physician workflow when prescribing opioids.

Benefits vs. Risks of Intraosseous Vascular Access

The Case

A 72-year-old woman with a history of asthma, congestive heart failure, and medication noncompliance presented to the emergency department with 2 weeks of lower extremity edema, fatigue, and progressively worsening dyspnea. She reported shortness of breath at rest and with exertion, as well as a dry cough. On initial examination, she was wheezing and had notable right lower extremity erythema and bilateral lower extremity pitting edema greater on the right side with weeping from her skin. She was admitted for asthma exacerbation and lower extremity cellulitis. She improved with fluids, albuterol nebulizers, methylprednisolone, and ceftriaxone/doxycycline. During her next 2 hospital days, she had a lower extremity ultrasound that was negative for a deep vein thrombosis and a transthoracic echocardiogram that was normal except for biatrial enlargement.

At midnight of her second hospital day, the patient's son noted that his mother was feeling dizzy. Four hours later, the patient suddenly became bradycardic to a heart rate of 20 beats per minute. Walking to the bathroom, she was notably dyspneic, with an oxygen saturation of 87%. She then became unresponsive. Her initial rhythm was pulseless electrical activity. During the code, a senior resident placed an intraosseous (IO) line in the left tibia following several unsuccessful attempts to obtain peripheral venous access. After 10 minutes of chest compressions and advanced cardiovascular life support protocol, spontaneous circulation returned and the patient was transferred to the intensive care unit (ICU).

Three hours after the IO line was placed, a nurse notified the primary team that the left leg was a dusky purple, and on examination the leg was bluish and tensely edematous with sluggish distal pulses. Vascular surgery diagnosed compartment syndrome, removed the IO line, and performed a bedside fasciotomy later that morning. The fasciotomy wounds were slow to heal and required ongoing complex care. After 2 months in the ICU and multiple complications, the patient was discharged.

Liver Biopsy: Proceed With Caution

The Case

A 42-year-old woman with a history of multiple malignancies, including osteosarcoma and recurrent breast cancer, presented to an emergency department with jaundice and epigastric pain. An abdominal ultrasound revealed several liver masses and subsequent imaging was consistent with metastatic malignancy of unknown primary source. The patient was admitted directly for an ultrasound-guided liver biopsy. Prior to the procedure, the patient required platelet transfusions, which increased her admitting platelet count of 5000/μL to 71,000/μL (reference range: 150,000–400,000/μL) prior to biopsy. Immediately after the procedure, she was transferred to the floor and began complaining about new abdominal pain. Her blood pressure was noted to be lower than baseline at 88/55 mm Hg, so a call was placed to the covering in-house physician. The physician believed that pain was common after such biopsies and ordered a dose of analgesics, which improved the patient's symptoms.

Over the next 2 hours, the patient's pain worsened and she became increasingly somnolent. When the bedside nurse returned to assess her pain, she found the patient unresponsive and called a code blue. The patient had pulseless electrical activity and the initial assessment also revealed a hematocrit of 14%, a decrease from 28% before the procedure. A massive transfusion protocol was initiated. The patient had a prolonged resuscitation and was transferred to the intensive care unit where she later died of multi-organ failure. The delay in recognizing the post-procedure intraperitoneal hemorrhage led to a detailed review by the hospital's quality committee. The protocols for managing patients following a liver biopsy were noted to be clearer in the outpatient setting where most procedures take place. No such protocols were in place for the less common inpatient liver biopsy at this facility.

Pitfalls in Diagnosing Necrotizing Fasciitis

The Case

A 49-year-old previously healthy man presented to the emergency department (ED) after falling from his truck at work 3 days before. He had gone to a different ED the day prior with diffuse pain on his left side (the side of his impact) and was given nonsteroidal anti-inflammatory medications and sent home. He presented to this new ED with persistent and worsening left arm, chest, abdomen, and thigh pain.

On physical examination, he was afebrile but tachycardic. He had diffuse, tender ecchymoses involving his left shoulder, upper chest, lateral abdomen, and thigh. Although the ED physicians felt he had simple bruising from the fall, they noted that he was in severe pain requiring intravenous (IV) opiates and that he was unable to independently ambulate. Because of these symptoms, blood tests were obtained and results showed a white blood cell count of 2.8×10^9/L (normal range: $3.5–10.5 \times 10^9$/L) and acute renal insufficiency with a creatinine of 1.4 mg/dL (normal range: 0.6–1.2 mg/dL). A computed tomography scan of the abdomen and pelvis showed "induration in the left quadriceps muscle and fluid layering in the abdominal wall." He was seen by the trauma surgical service, who felt the findings were due to diffuse bruising. The patient was admitted to an internal medicine service.

Due to ED crowding, he remained in the ED overnight, receiving only IV fluids and opiates for his pain. Over the course of the night, his pain worsened and he had a persistent tachycardia. Early morning lab

results showed a white blood cell count of 1.6×10^9/L, a creatinine of 1.6 mg/dL, a creatine kinase of 2650 U/L (normal range 55–170 U/L) (evidence of muscle breakdown), and a lactate of 6.2 mg/dL (normal range 0.5–2.2 mmol/L) (evidence of tissue hypoxia). He was seen by the internal medicine team mid-morning and diagnosed with rhabdomyolysis from trauma and acute renal failure. He continued to receive IV fluids. His pain had become so severe that he was switched to hydromorphone hydrochloride, administered through a patient-controlled analgesia pump.

Later that day, the patient had progressive respiratory distress and developed septic shock. He was re-evaluated by the surgical service and felt to have probable necrotizing fasciitis with pyomyositis. He was urgently taken to the operating room, where he required debridement of 7300 cm/sq (an area roughly 2 ft by 4 ft) of skin and soft tissue from his left arm and axilla, anterior chest wall, abdominal wall, thigh, and leg.

After surgery, he was progressively hypotensive despite multiple vasopressors. He developed multi-organ dysfunction and ultimately, after discussions with his family, care was withdrawn and he died peacefully. He underwent autopsy, which showed necrotizing fasciitis with pyomyositis secondary to methicillin-resistant *Staphylococcus aureus*.

CVC Removal: A Procedure Like Any Other

The Case

A 27-year-old man with a history of Behçet disease and recurrent liver abscesses was admitted to the hospital for a prolonged intravenous antibiotic course for treatment of the abscesses. Due to difficult peripheral venous access, a right internal jugular central venous catheter (CVC) was placed. After completion of the antibiotic course, the CVC was removed and the patient was discharged 30 minutes later. He subsequently experienced acute onset of shortness of breath associated with a "whistling sound" from his neck. He re-presented to the emergency department with hypoxia and a significant Alveolar–arterial gradient, requiring 15 L high-flow oxygen to maintain his oxygen saturation. A tentative diagnosis of air embolism was made, and computed tomography of the chest did not reveal other abnormalities that would explain his hypoxia, such as pulmonary embolism, pneumonia, pulmonary edema, or pneumothorax. The patient had a brief stay in the intensive care unit and improved rapidly.

On review of the case, it was determined that the CVC had been removed while the patient was in an upright position, and that the removal site was not covered with an occlusive dressing. The physician who removed the CVC had completed the required central line training module a year earlier, which included one slide on proper removal technique. The physician was not aware that the hospital CVC removal protocol specified the use of a CVC removal kit, and that the kit was available on the ward. The kit contained instructions for the procedure and the appropriate materials, including the occlusive dressing.

May I Have Another?—Medication Error

The Case

A 40-year-old man was admitted to the hospital after having a seizure. Upon admission, the patient, a pharmacology-trained research PhD, stated that this was his first seizure. His review of symptoms and physical examination were unremarkable. He denied the use of alcohol, caffeine products, and other recreational drugs; his only regular medications were multivitamins. He did volunteer that he typically had difficulty falling asleep, often taking a single dose of diphenhydramine 25 mg at bedtime. He noted that the diphenhydramine made him somewhat drowsy, but not enough to fall asleep.

In further discussion with the patient, he revealed that these sleep difficulties had substantially increased in the past few weeks to the point that he self-referred to a local sleep disorder program. During his first visit to the program, he was given a prescription for zolpidem. The patient brought the medication to the hospital; review of the label confirmed that the prescription was for zolpidem 10 mg. The printed instructions stated, "Zolpidem 10 mg, 1 at bedtime; if ineffective, take another." Based on his interpretation of these instructions, the patient revealed that he had been regularly taking up to 10 tablets of zolpidem every night and had recently ran out of his supply. A few days after abruptly stopping the medication, he experienced the seizure.

Wandering Off the Floors: Safety and Security Risks of Patient Wandering

The Case

A 74-year-old man with a history of congestive heart failure (CHF) secondary to alcoholic dilated cardiomyopathy was admitted for management of alcohol withdrawal. After several days of aggressive treatment, the patient was improving and was being managed on the medical-surgical floor. Initially he had been confused in the setting of alcohol withdrawal, but by hospital day 6 his mental status was clear and the patient was nearing discharge.

On the morning of hospital day 6, the patient was feeling "cooped up" and "needed a change of scenery" and a cigarette. He wandered off the floor without informing his bedside nurse or any other health care provider, and he left the hospital grounds.

When he returned to his room an hour later, the patient complained of new right arm pain. He was examined and the physician found evidence of diffuse bruising of his right arm. A subsequent radiograph revealed a fractured humerus (bone of the upper arm). After the radiography results were revealed to the patient, he acknowledged that he had fallen while he was off the floor.

He was treated for his fracture and the institution began to consider a policy regarding patients leaving the unit while hospitalized.

Discontinued Medications: Are They Really Discontinued?

The Case

A 69-year-old man with a history of chronic atrial fibrillation and associated cerebrovascular accident (CVA) treated with warfarin and aspirin, presented to the emergency department (ED) with a severe headache. A STAT computed tomography (CT) scan revealed bilateral subdural hematomas. His international normalized ratio (INR) was determined to be supratherapeutic at 4.9. He was admitted to the intensive care unit (ICU) for monitoring of his neurologic status. After resolution of the severe headache, warfarin was restarted because of the high risk associated with his previous CVA (CHADS2 score of 3).

One day after re-initiation of his warfarin, he experienced a recurrence of his subdural hematoma. The warfarin was discontinued, the patient stabilized clinically, and he was later discharged home. Although warfarin was not included on his Discharge Medication list, a few days after returning home the patient received warfarin via mail order from his outpatient pharmacy. While confused by the receipt of the warfarin, the patient restarted the medication. At his follow-up appointment he was noted to have an elevated INR. Recognizing the elevated INR was a result of the patient's re-initiation of warfarin, a repeat head CT was performed which fortunately was negative for recurrent hemorrhage. In response to these events, warfarin was added to his allergy list with the comment "Never to be resumed." Regardless, when the primary care provider (PCP) contacted the pharmacy weeks later, warfarin remained on the active medication list, with available refills. The PCP had it removed from this list.

Raise the Bar

The Case

A 57-year-old man presented to an ambulatory surgery center for excision of a right groin lipoma. The patient was seen and evaluated by an anesthesiologist who was new to the center. After discussing anesthetic options with the patient, the physician proceeded with regional anesthesia and performed a right iliac block in the preoperative holding area. The patient was then taken to the operating room, where he awaited the arrival of the surgeon. Without alerting the nurse, the patient tried to get up to use the restroom, but—because his leg was now numb—fell and hit his head on the ground. After hearing the fall, the nurse came quickly to evaluate and, given complaints of acute neck pain, the patient was transferred to the local emergency room. A heated interaction ensued between the anesthesiologist and nurse around why certain safety measures hadn't been taken to protect the patient. Ultimately, the patient didn't experience any significant injury and he had his lipoma removed the following week.

The quality review committee at the ambulatory surgery center investigated the events. It was noted that the rails of the patient's bed were not raised after the block was placed, largely because the nurses were unaware that the procedure had been performed by the anesthesiologist. Because of this poor communication, the nurse assumed that the block would be placed in the operating room (as was done by other anesthesiologists on staff). Moreover, she reported being unfamiliar with the use of regional blocks in general.

Medication Reconciliation With a Twist (or Dare We Say, a Patch?)

The Case

An 80-year-old woman with a history of dementia was admitted to the hospital with abdominal pain and diagnosed with a bowel obstruction, secondary to a new diagnosis of colon cancer. She underwent an uncomplicated surgical resection of the colon cancer with relief of the obstruction. Postoperatively she developed confusion and agitation consistent with acute delirium.

At this hospital, a geriatric psychiatry consulting service was available to help manage postoperative delirium and was consulted by the surgical service. As part of their evaluation, they reviewed the patient's current and prior medications to determine possible triggers and optimize treatment. They spoke directly with the family and reviewed the official medication reconciliation list, which a pharmacist had documented at admission. Although the family stated that the patient was on a "memory medicine," the reconciliation list did not include any dementia medication. Based on this discrepancy, the consulting service contacted the outpatient pharmacy and learned the patient was prescribed a cholinesterase inhibitor patch (a medication for dementia), to be replaced weekly. She had not been prescribed the drug during the hospital stay, and the last patch had been placed more than a week earlier. Although many factors likely contributed to postoperative delirium, the geriatrics service felt that abrupt withdrawal of the cholinesterase inhibitor contributed to the episode.

CYP450 Drugs: Expect the Unexpected

The Case

A 42-year-old man with acquired immunodeficiency syndrome (AIDS) (CD4 count 198), hip dystocia, and generalized anxiety disorder presented with acute sciatic pain. His human immunodeficiency virus (HIV) regimen (ritonavir-boosted darunavir, tenofovir, and emtricitabine) had been stable, resulting in an undetectable blood plasma viral load. In addition to his antiretroviral therapy, he was also taking clonazepam and escitalopram. After review by his primary care provider, the patient was referred to a

spine orthopedist for management of his sciatica. A hip replacement had also been planned for his dystocia, but the sciatica resulted in a delay for his hip arthroplasty.

In response to his complaints, the spine surgeon elected to administer a single injection of epidural triamcinolone. However, one week after the injection, the patient returned to the surgeon's office complaining of fever, anxiety, nausea, abdominal pain, and insomnia. The surgeon advised the patient that these symptoms were not related to the epidural injection or the sciatic pain and referred the patient back to his internist. One week later, the patient was reexamined by the internist and found to have an elevated blood pressure (156/96 mm Hg), anxiety, 5-pound weight gain, and epigastric tenderness. *Helicobacter pylori* screening, HIV lab work, complete blood count, and chemistry screen revealed a decreased CD4 count to 98, nonfasting blood sugar of 166 mg/dL, and a positive urea breath test [a screening test for *H. pylori*]. One week of appropriate *H. pylori* treatment resulted in no improvement in symptoms; in fact, the patient complained of increased insomnia, anxiety, sweats, and weight gain. The diagnosis of Cushing syndrome was considered, and subsequent testing for this syndrome was positive.

The physicians later recognized that HIV medications, particularly ritonavir-associated therapy, are associated with substantial numbers of drug–drug interactions. Ritonavir induces cytochrome P450 (CYP1A2); however, it inhibits the major P450 isoforms (3A4 and 2D6). It was determined that triamcinolone is a 3A4 substrate, and ritonavir has been implicated in Cushing syndrome following oral and other routes of synthetic corticosteroid administration. The spine surgeon had only noted that the patient "is on HIV medication and stable" and did not review each individual medication. In addition, the spine surgeon did not provide a consultation report to the internal medicine team and primary care provider regarding the steroid injection. Only after the medicine and HIV teams questioned the patient regarding recreational steroid use did the patient reveal his recent epidural therapy.

The patient experienced 4 weeks of Cushing-like symptoms, including abdominal pain, insomnia, impotence, anxiety, sweats, and nausea; symptoms improved after adjustment of his HIV medications. These post-epidural events delayed his hip replacement surgery by several months.

Clostridium Difficile Relapse Secondary to Medication Access Issue

The Case

A 24-year-old woman with history of HIV/AIDS [human immunodeficiency virus/acquired immunodeficiency syndrome] and diffuse B-cell lymphoma, actively receiving chemotherapy, was admitted with diarrhea and abdominal pain. The patient reported recent antibiotic use, and a stool sample was positive for *Clostridium difficile* toxin. As she had prior episodes of *Clostridium difficile*–associated diarrhea (CDAD), she was treated with oral vancomycin. She improved quickly and was discharged with a plan to complete a 14-day course of oral vancomycin. After being discharged, the patient took her discharge prescriptions to her usual retail pharmacy. However, the pharmacy informed her that the oral vancomycin solution had not been approved by her insurance, and she was unable to afford the considerable cost of paying for the medication out of pocket.

The patient contacted her primary care physician, and over the next 4 days, the nurses at the patient's primary care clinic spent many hours on the phone attempting to obtain coverage for the vancomycin solution. Despite contacting the medical director of the insurance plan, the approval was never finalized and during this time the patient received no treatment. Soon, her symptoms recurred. She was instructed to return to the emergency department, where a computed tomography scan was suggestive of toxic megacolon (marked dilation and inflammation of the colon secondary to uncontrolled infection). She was readmitted and re-started on oral vancomycin and intravenous metronidazole for treatment of severe

CDAD. Fortunately, she improved with this regimen and did not require surgery. The plan again was to discharge her with a long course of oral vancomycin with a taper, as per the infectious disease service's recommendation.

During the readmission, a pharmacist was consulted in order to help the patient gain access to oral vancomycin in advance of discharge. The pharmacist contacted the patient's insurance and was informed that the vancomycin oral solution could only be filled at a compounding pharmacy, and that the patient's usual retail pharmacy (part of a national chain) could not perform this service. Eventually, after much effort, an independent pharmacy was identified that could compound the medication and was contracted with the patient's insurance. Given the issues after her prior hospitalization, the patient remained hospitalized until a clear plan was in place to ensure her access to medication.

The independent pharmacy filled the oral vancomycin solution, which was delivered to the patient, and she was able to complete her treatment course. However, after the second discharge the inpatient pharmacist was contacted by the pharmacist at the patient's usual retail pharmacy. The outpatient pharmacist informed the inpatient pharmacist that a prescription for vancomycin oral capsules (not vancomycin solution) could have easily been filled after the initial discharge and would have been covered by the patient's insurance. Had this information been available, the patient might have been able to access the medication after the first discharge, potentially avoiding the patient's return of symptoms, the readmission, and the subsequent treatment costs.

A "Reflexive" Diagnosis in Primary Care
The Case

A 54-year-old man with no significant past medical history presented to a new primary care physician complaining of 2 years of progressive bilateral hand and foot paresthesias, pain, and weakness. Due to these symptoms, he had multiple falls and an inability to grasp simple objects. At the time, the primary care doctor documented 4/5 weakness in all extremities and a loss of sensation in his hands and feet bilaterally. Based on this, the patient was diagnosed with a peripheral neuropathy (a loss of sensation that typically begins in the hands and feet) and referred to see a neurologist sometime in the next 3 months.

Over the next 10 weeks, the patient returned 2 more times to the same clinic with worsening symptoms, including more frequent falls and new back pain. He saw two different providers who did not order any additional diagnostic testing and treated him supportively, assuming his symptoms were due to the previously diagnosed peripheral neuropathy.

When he was finally seen in the neurology clinic, the exam revealed hyperreflexia and increased tone in all extremities. This was most consistent with a spinal cord process and not a peripheral neuropathy. The neurologist ordered an urgent magnetic resonance imaging (MRI) of the spinal cord, which revealed critical cervical (neck) cord compression, so tight that it placed the patient at risk for permanent paralysis. He was admitted to the hospital and underwent urgent neurosurgical decompression.

Unfortunately, likely due to the delay in making the diagnosis and surgery, the patient still has some weakness in his legs and persistent nerve pain.

A root cause analysis of the case revealed that none of the doctors who had seen the patient had performed an exam of the reflexes or assessed for overall muscle tone. The safety committee felt if these components of the exam had been performed, the providers may have arrived at the diagnosis earlier or may have made a more urgent referral to neurology.

Late Anemia Following Rh Disease in a Newborn

The Case

A full-term neonate was delivered uneventfully to an Rh-negative woman who had received RhoGAM (Rho[D] immunoglobulin treatment) at 28 weeks. The neonate developed hyperbilirubinemia within 24 hours of delivery, which prompted initiation of aggressive phototherapy. He also received two blood transfusions and two doses of intravenous immunoglobulin in the neonatal intensive care unit. These therapies were given to prevent the need for a more risky exchange transfusion. On discharge at day-of-life (DOL) 10, hemoglobin and bilirubin levels were stable. The treatment plan was for regular blood draws to assess the ongoing stability of hemoglobin and bilirubin levels.

Over 3 visits in the subsequent 10 days, the patient was seen by different providers who all noted that the hemoglobin remained stable at 12 g/dL, and the bilirubin continued to fall. These reassuring trends were noted in the record. On DOL 25, the bilirubin maintained its downward trend, but the hemoglobin was also noted to have dropped to 10 g/dL. Given the bilirubin was decreasing, the providers were reassured and no additional lab draws were scheduled.

Two days later, the family brought the infant back to the urgent care clinic with unrelated concerns about redness around the umbilicus. Noting the reduction in hemoglobin from the last visit, a repeat hemoglobin test was ordered that came back even lower: 7.7 g/dL. The clinicians now recognized that the infant had active Rh hemolytic disease, and he was admitted to the hospital for blood transfusion and close monitoring. Due to the readmission and the family's frustration with the inconsistent care provided since the first discharge, the case was reviewed by the pediatric quality committee. While many communication concerns were identified, the key issue was the management of an uncommon disease using markers that are frequently trended for common conditions. The patient improved and he ultimately did well with appropriate therapies.

After-Visit Confusion

The Case

An otherwise healthy 18-year-old woman presented to an urgent care clinic with new bumps and white spots near her tongue. The patient's mother accompanied her and expressed concern that this could be "thrush"—based on her own understanding of that condition. The patient was examined and noted to have small white ulcerations at the base of her tongue and one on the left buccal mucosa. The symptoms developed a few days following an upper respiratory infection. The rest of the examination was unremarkable. The physician explained that this was likely herpetic gingivostomatitis and provided related information about the condition and its treatment plan. The patient was then discharged from the urgent care clinic and provided an after-visit summary that is generated from their electronic medical record (EMR). The written materials outline the diagnosis, care plans, and follow-up needs, all of which were reviewed by the medical assistant.

After returning home, the patient's mother continued searching her daughter's condition online, remained concerned about the possibility of thrush, and sent a couple of messages to the provider via a patient portal within the EMR. One particular issue was that the after-visit summary stated that the patient's diagnosis was thrush, despite the physician stating an alternate diagnosis. Ultimately, the physician spoke with the patient's mother, confirmed that his diagnosis of a herpetic viral infection was correct, apologized for the error on the after-visit summary, and reassured her that the condition was self-limited and would improve, which it did. Although no harm resulted from the interactions, the mistake on the after-visit summary and the communication discrepancies it generated led to a number of unnecessary phone calls and follow-up communications, not to mention understandable distress to the patient and her mother. The

after-visit summary incorrectly populated the diagnosis of thrush from the triage information and it was not updated after the actual evaluation by either the physician or the medical assistant.

Tough Call: Addressing Errors From Previous Providers

The Case

A 55-year-old woman with a history of type 2 diabetes on metformin presented to the emergency department (ED) with 3 days of progressive malaise, diffuse abdominal pain, and nausea and vomiting. On presentation, she was afebrile, tachycardic, and hypotensive, with normal oxygen saturation. Her laboratory data was notable for an elevated white blood cell (WBC) count of 23,000/mm^3, acute kidney injury with an elevated creatinine of 2.2 mg/dL (up from a baseline of 0.8 mg/dL), and a severe metabolic acidosis secondary to lactic acidosis, with a pH = 7.05 with a lactate of 18 mmol/L (normal 0.5–1.6 mmol/L).

Based on her clinical presentation, she was treated for severe sepsis and given intravenous fluids and antibiotics. In reviewing her medical record, the admitting team noted she had been admitted 3 times in the last 2 months with the identical clinical presentation. Each time she had been diagnosed with sepsis even though no clear source of infection had been found, and each time she had improved and was discharged after 5 days in the hospital. In addition, during two of those hospitalizations, she required mechanical ventilation from pulmonary edema and volume overload from getting aggressive fluids to treat her "sepsis."

The admitting team re-examined all of the information and realized the clinical presentation was not consistent with sepsis; rather, it was far more consistent with acute lactic acidosis secondary to metformin (a well-recognized complication of metformin treatment). The metformin and antibiotics were stopped, and she was treated conservatively and did well. The metformin was added to her allergy list, and, since stopping, she had no further episodes.

The attending physician on the admitting team wondered why the diagnosis had not been made during the previous admissions. Although the degree of illness and lactic acidosis could be consistent with sepsis, no clear source of infection had been discovered; recurrent sepsis without a source is highly unlikely. In addition, the degree of lactic acidosis was out of proportion to the degree of illness, which should have prompted exploration for other causes of severe lactic acidosis (i.e., metformin). She felt like this was a diagnostic error—that the multiple clinicians and teams who had cared for the patient had likely "anchored" on the diagnosis of sepsis and didn't consider other possibilities. She wondered what to do. What was the most effective way to give feedback to the previous teams? Should the providers be blamed for possibly missing the diagnosis? Because the patient likely experienced harm because of the error, should anyone be punished? What could be done to prevent this from happening in the future?

An Easily Forgotten Tube

The Case

A 45-year-old man was admitted to the intensive care unit (ICU) for acute liver failure secondary to alcohol abuse. His illness was complicated by acute renal failure requiring dialysis and by respiratory failure requiring intubation, as well as hepatic encephalopathy requiring therapy with lactulose. A rectal tube was inserted on hospital day 7 for management of diarrhea that occurred with lactulose therapy. Over the course of his ICU stay, the patient's encephalopathy improved and he was weaned from mechanical ventilation and extubated.

On hospital day 9, he was transferred out of the ICU to a general medicine floor for continued care. His mental status improved and his serum ammonia decreased. Although lactulose was discontinued, the patient's diarrhea persisted. He passed a swallowing evaluation, made significant progress with physical and occupational therapy, and was recommended for eventual transfer to an acute rehabilitation facility. On hospital day 13, the patient was incidentally noted to have an internal jugular deep vein thrombosis, likely related to previous temporary dialysis catheter placement. An intravenous heparin infusion was started. On hospital day 14, the patient's hemoglobin dropped by 2 g/dL, and dark red liquid stool was noted in the rectal tube. The heparin infusion was stopped, and the patient was transfused with two units of packed red blood cells. On hospital day 15, the patient underwent colonoscopy, which revealed a large area of ulcerated mucosa comprising half the circumference of the rectum, likely caused by the rectal tube.

After discussion of the risks and benefits, the heparin infusion was discontinued. The patient did not require an increased level of care, but his inpatient stay was prolonged, and he received both transfusion and the colonoscopy because of the rectal ulcer.

Nonsustained Ventricular Tachycardia After Acute Coronary Syndromes: Recognizing High-Risk Patients

The Case

A 51-year-old woman with coronary artery disease, diabetes, and hypertension was admitted with a non-ST elevation myocardial infarction (NSTEMI) and underwent percutaneous coronary intervention (PCI). After uncomplicated placement of two stents, she was transferred to the telemetry unit. About 12 hours after the procedure, the patient's nurse noted a five-beat run of ventricular tachycardia (VT). The patient was asymptomatic and other vital signs were stable. The nurse called the responsible physician who responded that "this was expected" (given her underlying heart disease and perhaps the possibility of reperfusion arrhythmias). The patient had several more short runs of non-sustained ventricular tachycardia (NSVT). However, given the physician's initial response, the nurse did not notify the physician about these additional runs. About 2 hours after the initial run of VT, the patient experienced a cardiac arrest secondary to sustained VT. She underwent cardiopulmonary resuscitation including chest compressions and defibrillation. Though the patient survived the initial arrest, she remained hypotensive and unfortunately did not regain any meaningful neurological function. Care was ultimately withdrawn 4 days after the event.

Multifactorial Medication Mishap

The Case

A previously healthy 50-year-old man was hospitalized while recovering from an uncomplicated spine surgery. Although he remained in moderate pain, clinicians planned to transition him from intravenous to oral opioids prior to discharge. The patient experienced nausea with pills but told the bedside nurse he had taken liquid opioids in the past without difficulty.

The nurse informed the physician that the patient was having significant pain, and liquid opioids had been effective in the past. When the physician searched for liquid oxycodone in the computerized prescriber order entry (CPOE) system, multiple options appeared on the list—two formulations for tablets and two for liquid (the standard 5 mg per 5 mL concentration and a more concentrated 20 mg per mL formulation). At this hospital, the CPOE system listed each choice twice, one entry with the generic name and one entry with a brand name. In all, the physician saw eight different choices for oxycodone products. The physician chose the concentrated oxycodone liquid product, and ordered a 5-mg dose.

All medication orders at the hospital had to be verified by a pharmacist. The pharmacist reviewing this order recognized that the higher concentration was atypical for inpatients but assumed it was chosen to limit the volume of fluid given to the patient. The pharmacist verified the order and, to minimize the risk of error, added a comment to both the electronic medication administration record (eMAR) and the patient-specific label that the volume to be given was 0.25 mL (5 mg). For added safety, the pharmacist personally retrieved, labeled, and delivered the drug and a calibrated syringe to the bedside nurse to clarify that this was a high concentration formulation for which the volume to administer was 0.25 mL (a smaller volume than would typically be delivered).

Shortly thereafter, the nurse went to the bedside to administer the drug to the patient for his ongoing pain. She gave the patient 2.5 mL (50 mg) of liquid oxycodone, a volume that she was more used to giving, and then left for her break. A covering nurse checked on the patient and found him unconscious—a code blue was called. The patient was given naloxone (an agent that reverses the effect of opioids), and he responded well. He was transferred to the intensive care unit for ongoing monitoring and a continuous infusion of naloxone to block the effect of the oxycodone. By the following morning, the patient had returned to his baseline with no apparent adverse effects.

SNFs: Opening the Black Box

The Case

An 88-year-old woman was admitted to a skilled nursing facility (SNF) after a lengthy hospitalization for a small bowel obstruction, acute renal failure, and deep vein thrombosis. On arrival to the SNF, the patient was on 14 medications for her various conditions and remained mildly delirious. Nursing staff at the SNF expressed concerns about the level of care that could be provided, but they were told that the patient "didn't meet inpatient criteria any longer." During the first few days of the SNF visit, the staff continued to express concerns about the patient's overall health because she was not able to take all of her medications. The family was also concerned. The SNF physician saw the patient on the first day but not after that time. He continued to manage questions via phone with the nursing staff. About 3 days after admission, the patient developed a fever and shortness of breath, prompting a 911 call and transfer back to the acute facility. There, she was diagnosed and treated for pneumonia.

Check the Anesthesia Machine

The Case

A 62-year-old man with weight of 134 kg (body mass index [BMI] of 40) and history of hypertension, diabetes, sleep apnea, claustrophobia, and 3-vessel coronary artery disease was scheduled for elective coronary artery bypass surgery. Once in the operating room, the resident placed an arterial line in the patient's left arm under local anesthesia. Because the patient was unable to tolerate the facemask oxygen (due to claustrophobia), the attending anesthesiologist gave him the anesthetic circuit, which had oxygen flowing at 10 liters per minute and asked him to keep it in his mouth and breathe through it (like snorkeling) to achieve pre-oxygenation. The anesthesiologist then injected 2 mg of midazolam to sedate the patient.

After about 5 minutes, the anesthesia team noticed that the patient was unresponsive, with shallow breathing. Breathing was assisted with facemask ventilation and the airway was secured with endotracheal tube (after propofol, fentanyl, and rocuronium rapid induction). Once anesthesia was induced, the anesthesiologist tried to turn on the anesthetic agent and noticed that the desflurane vaporizer was set to 12%. It was then discovered that the patient had inadvertently received 12% desflurane (a general anesthetic) instead of oxygen alone during pre-oxygenation. The logbook on the anesthesia machine showed that the machine had been checked that morning, but the resident had failed to notice the

open desflurane vaporizer. The patient did not experience any obvious harm from the uncontrolled inhalation induction.

New Oral Anticoagulants
Case & Commentary—Part 1

A 39-year-old woman with a history of deep venous thrombosis (DVT) underwent an uncomplicated knee replacement. For pain control after surgery, an epidural catheter was placed. The patient's pain was well controlled with the catheter, which was managed by the pain service at this hospital. (Often used for pain control after orthopedic surgery procedures of the lower extremities, epidural catheters infuse analgesics such as lidocaine or opioids into the epidural space around the spinal cord. Anticoagulants are contraindicated at the time of insertion or removal due to bleeding risk.)

The patient had been on rivaroxaban (a relatively new oral anticoagulant) as treatment for her DVT before admission, and thus the discontinuation of anticoagulation placed her at high risk for recurrent DVT or pulmonary embolism. Per standard protocol, she was given enoxaparin (an anticoagulant injected subcutaneously) after surgery as a "bridge" until she could resume her oral anticoagulant. On the second hospital day, she was started on her outpatient dose of rivaroxaban.

For the past 60 years, vitamin K antagonists such as warfarin sodium have been the only available oral anticoagulant medications. More recently, target-specific oral anticoagulants (TSOACs) have become available for the treatment and prevention of thromboembolism and currently make up approximately 20% of new anticoagulant prescriptions.(1-4) There are currently three FDA-approved TSOACs: the direct thrombin inhibitor dabigatran (Pradaxa) and two factor Xa inhibitors, rivaroxaban (Xarelto) and apixaban (Eliquis). TSOACs work further down the clotting cascade and have more specific targets of inhibition than warfarin, leading to several advantages: fixed-dose oral dosing, fewer drug–drug and dietary interactions, and no need for routine coagulation monitoring (Table).(5,6) At present, all three are approved for use in preventing stroke in patients with atrial fibrillation. Rivaroxaban is also approved for the treatment and prevention of venous thromboembolism, such as in the case of this patient. We do not have information to explain why she was taking rivaroxaban instead of warfarin, but patients and providers may sometimes prefer using TSOACs due to the ease of administration and to avoid the monitoring needed when taking warfarin. The rivaroxaban was appropriately held before her surgery and then restarted on the second hospital day, presumably when the surgeon believed the risk of bleeding was low enough to tolerate anticoagulation.

Data from large randomized trials comparing TSOACs to warfarin largely conclude that TSOACs are at least as effective as warfarin in patients with atrial fibrillation and venous thromboembolism, and have similar, if not lower rates, of serious hemorrhagic complications (e.g., intracranial hemorrhage, gastrointestinal bleeding).(1,2) TSOACs all result in an increased risk for hemorrhage but, unlike warfarin, have no clinically-proven antidotes as of yet. In other words, there is no proven way to reverse the anticoagulation for any of the TSOACs. Patients who orally ingest a TSOAC are actively anticoagulated within several hours and, because the half-life of TSOACs is considerably shorter than that of warfarin, most of the anticoagulant effect will typically wear off within 1–2 days.(5) TSOACs are cleared, to varying degrees, by the kidneys, and patients with impaired renal function were largely excluded from clinical trials. Renal insufficiency can delay clearance of anticoagulant effect and TSOACs are not recommended in patients with severe renal insufficiency (e.g., creatinine clearance

Case & Commentary—Part 2

A few hours after receiving her third dose of rivaroxaban, the fellow on the pain service came to remove the epidural catheter. As was his usual practice, he scanned the medication list to be sure the patient was not on enoxaparin or warfarin or other traditional anticoagulants, but he did not review the rest of the list. He removed the epidural catheter while the patient was receiving treatment doses of rivaroxaban, placing her at very high risk for bleeding and the development of an epidural hematoma (the guidelines at this hospital stated that epidural catheters should not be removed for at least 24 hours following a dose of rivaroxaban).

Later, when writing his note about the procedure, he glanced at the medication list and noticed the patient was on rivaroxaban. He immediately examined the patient who was feeling well and had no back pain or weakness. The surgical team and pain service disclosed the error to the patient and monitored her very closely for the development of any complications. Fortunately, the patient did not have any apparent bleeding and was discharged in good condition.

Because TSOACs have only had FDA approval for 2–3 years, many clinicians may be unfamiliar with their use and properties. There is especially little information about the optimal management of TSOACs around the time of invasive procedures.(7) Patients undergoing neuraxial anesthesia (e.g., the epidural catheter used in this case) are at risk for developing rare but devastating bleeding around the spinal cord when exposed to anticoagulants. Recent guidelines from the American Society of Regional Anesthesia and Pain Medicine recommend that TSOACs be stopped for 2–4 days (depending on which of the three was used) before initiation of neuraxial anesthesia, and recommend against administration of a TSOAC while a catheter is in place, if possible, or to delay removal of a catheter until the anticoagulant effect is minimal.(8,9) Resumption of TSOACs should not be attempted for at least 6 hours after a catheter is removed. Individual institutions may have slightly different recommendations.

Although this patient did not experience any harm, the above situation would be characterized as a near miss. Two factors increased the likelihood of error in this situation: (i) the limited clinical experience with TSOACs among many clinicians; and (ii) the lack of a "safety net" system in place that could systematically identify and potentially catch errors related to high-risk medications.

Common Errors Related to TSOAC Use

A number of potential errors may occur related to TSOAC use.(10) The first is prescribing to inappropriate patients. Examples include prescribing TSOACs to a patient with severe renal insufficiency or using TSOACs for non-approved indications (e.g., mechanical heart valves). TSOACs may also not be appropriate for patients who have a very high bleeding risk, such as in the situation above or in patients with recent large hemorrhage at risk for recurrent hemorrhage.

Another potential error is inappropriate dosing or administration. TSOACs vary by their pharmacokinetics and elimination half-lives, and clinicians may not be aware of when to stop or start these medications in specific clinical situations, such as the perioperative period. In addition, unlike warfarin, which has a long half-life (thus patients remain anticoagulated even if a dose is missed), a missed dose of a TSOAC can be devastating because of these agents' relatively short half-lives. TSOACs now have black-box warnings informing clinicians that thromboembolism risk increases with abrupt discontinuation of the medication.(11)

Inappropriate monitoring also creates potential for error. Clinicians may inappropriately order coagulation tests that do not correlate with TSOAC effect. For example, commonly obtained tests for warfarin or heparin, including the prothrombin time or partial thromboplastin time, do not accurately measure TSOAC activity. Or, they may also fail to order TSOAC-specific tests when such tests are indicated, as in

situations in which it is important to assess residual anticoagulant effect. For example, obtaining a thrombin time may be appropriate to determine whether there is residual dabigatran effect in a patient who did not remember when he last took his medication (Table).

Institutions should consider implementing interventions that address some of these common errors related to TSOAC use. Promoting awareness of new guidelines and updating medical knowledge among clinicians is certainly a component of effective interventions but is rarely sufficient to drive behavior change on a large scale.(12,13) Implementing system-level interventions, such as incorporating best practice or preferred prescribing recommendations into standardized order-sets or workflows, are considerably more effective than education alone. Information technology–based solutions, such as computerized "best practice alerts" that appear when a TSOAC is prescribed to patients with contraindications, can also help catch errors. Effective quality improvement interventions must also be supported by regular auditing of clinical practice paired with feedback to services and clinicians.

In the above case, the error may have been prevented if an automated best practice alert appeared when the clinician tried to order an anticoagulant in a patient with an epidural catheter. Ideally, institutions should be proactive about identifying problem areas related to high-risk medications (e.g., anticoagulants), performing periodic assessments of clinical practice, and developing system-level interventions to reduce the likelihood of errors where warranted. Often, these interventions require multidisciplinary input from medicine, nursing, and pharmacy.

Take-Home Points

- Target-specific oral anticoagulants (TSOACs) have become viable alternatives to conventional oral anticoagulants and have the advantages of fixed-dose oral dosing, relatively rapid onset and offset, and fewer drug–drug interactions compared with warfarin.
- Common errors related to TSOAC use include prescribing to inappropriate patients, recommending an inappropriate dose or administration, and inappropriate monitoring.
- Clinicians should be particularly cautious about administering TSOACs to patients at high risk for bleeding, including those undergoing neuraxial anesthesia (e.g., an epidural catheter).
- The rapidly evolving field of knowledge related to the use of TSOACs highlights the importance of developing institutional systems to improve awareness of these new agents and incorporate best practice standards into clinical workflow.

Finding Fault With the Default Alert

The Case

A 33-year-old man with known refractory epilepsy and developmental delay was admitted to the hospital after experiencing increased seizures. He previously had been well managed with levetiracetam (Keppra); however, therapy had been discontinued after the patient experienced a new rash. Once admitted to the hospital, his seizures were controlled with fosphenytoin. Discharged 2 days later, the outpatient plan was to begin phenytoin 500 mg once daily. However, the discharge prescription was erroneously written as phenytoin 500 mg "three times daily" (TID). His outpatient pharmacy filled this prescription and the patient subsequently took the medication at this frequency for 2 days. After noting the patient's difficulty in walking, his mother contacted the primary team, the error was identified, and the frequency of dosing corrected to "once daily."

In review of the resident's discharge note, the discharge plan for the phenytoin was clearly stated, i.e., "once daily." However the resident was relatively unfamiliar with the electronic medical record (EMR) and failed to notice that the EMR default frequency for phenytoin was "TID." While the error may be attributed to a "slip" by a busy resident who was unfamiliar with the computer ordering system, alert

fatigue also played a role. When a phenytoin dose much greater than normal is prescribed, the EMR triggers an alert for the clinician; this alert was overridden by the resident. Furthermore, it is likely that the hospital pharmacy similarly missed or overrode a dosing alert. Lastly, the community pharmacy did not question the 500 mg TID dosing regimen. Although the patient was inadvertently prescribed excessive phenytoin and experienced temporary toxicity, he experienced only temporary harm. As a result of this error, the hospital changed its default setting for phenytoin from TID to once daily.

Are You Mrs. A? An Issue of Identification Over Telephone

The Case

Mr. A was a 78-year-old man admitted with non-ST elevation myocardial infarction with acute kidney injury for whom medical management was chosen due to his multiple comorbidities. The patient's code status was DNR (do not resuscitate). Mr. B was a 62-year-old man admitted to the same medicine unit with hypoglycemia and a diabetic foot ulcer. He had a past medical history of ischemic cardiomyopathy. At 1:00 AM, the nurse found Mr. A unresponsive. The medicine intern was notified and pronounced Mr. A dead.

The intern went to the counter of the floor's central nursing unit to complete the death certificate and to notify the next-of-kin. The unit clerk usually put the death certificate folder on the counter next to the deceased patient's chart. This time, the chart next to the death certificate was Mr. B's chart. The intern grabbed Mr. B's chart, mistakenly believing that this was Mr. A's chart, and looked at the contact information on the front sheet. He called the number and notified Mrs. B that her husband had died. After erroneously notifying Mrs. B, he shifted his focus to completing the death certificate. It was at that point that he discovered that he had the wrong chart. He called Mrs. B back immediately, about 20 minutes after the previous call. Unfortunately, Mrs. B had called her children and let them know that their father had died. The intern apologized to Mrs. B and let her speak to her husband to reassure her. He then called Mrs. A and notified her about the death of her husband.

After being notified of the error, Mrs. B and her children were distraught after experiencing 20 minutes of thinking that their beloved husband/father had died.

A Picture Speaks 1000 Words

The Case

A 62-year-old man with a past medical history of hypertension, hyperlipidemia, and type A aortic dissection repair presented with chest pain at a community hospital. An aortic protocol computed tomography (CT) for dissection was ordered and performed, and the preliminary reading from the on-call resident was "no acute changes." Since the dissection was believed to be stable and a higher level of care appeared unnecessary, the patient was admitted to the medicine service of the hospital for further workup.

Six hours after the patient arrived to the medical floor, he developed increasing migratory chest pain, dyspnea, and diaphoresis. The medical team arrived to find him hypotensive, tachycardic, and minimally responsive, with unequal blood pressures in his arms. Despite intensive care unit transfer and aggressive life-saving interventions, he died a few hours later. Autopsy revealed proximal progression of the false lumen of his known type A dissection with rupture into the pericardial sac.

The case was reviewed in light of the tragic outcome. The hospital that cared for the patient was a federal facility affiliated with a large academic medical center. This facility had no in-house radiology services at night; thus, nighttime studies were sent electronically to on-call residents at the academic medical center. A data firewall had been constructed to "improve information security" at the federal facility, which

rendered the radiology residents unable to access previous studies, only the text reports of the studies. The barrier, which had initially blocked both text reports and actual radiology studies, was well known to the on-call radiology residents, and they had developed a workaround to allow them to access the text reports. In this particular case, the overnight read by the resident was based on a comparison of the current study with the results on the text report of the prior dissection. The following morning, an attending radiologist determined that a comparison of the new study and the prior images clearly demonstrated proximal progression of the dissection.

Following this case, data safety and monitoring policies were changed. Access to stored imaging was facilitated and the firewall was disabled. Informal enquiries with other federal institutions suggest that employment of such firewalls and security protocols is commonplace.

DRESSed for Failure

The Case

A 60-year-old woman who uses a wheelchair presented to the emergency department (ED) with right hand cellulitis and an uncomplicated urinary tract infection. The patient had a complicated medical history that included poly-substance abuse, hepatitis C, a mitral valve replacement, and multiple strokes, which left her non-verbal and fully dependent on caretakers for tasks of daily living. In the ED, she was treated with a dose of intravenous ceftriaxone and sent home with a prescription for oral cephalexin. One week later, the patient returned to the ED critically ill with hypotension, altered mental status, and an erythematous rash on her upper extremities. She was admitted to the intensive care and treated presumptively for sepsis. Dermatology was consulted to evaluate her desquamating rash and, on full chart review, they noted a previous diagnosis of drug rash with eosinophilia and systemic symptoms (DRESS) associated with cephalexin. High-dose steroids were administered and the patient's condition rapidly improved. She ultimately returned to her baseline condition and was discharged home with her caretaker.

In conducting a root cause analysis of the error, the patient's history of cephalexin-induced DRESS was only documented as an "allergy" in the previous electronic health record (EHR). The medical center recently transitioned to a new EHR, and the institution made a deliberate decision to have clinicians review all patient allergies "from scratch" rather than simply transfer the information over from the old system. However, despite a few ambulatory visits for this patient since transition to the new EHR, the allergy list was never updated to include cephalexin. Further complicating this particular case, because the affected patient was non-verbal with many caretakers over the past few years, history taking was unreliable.

The Pains of Chronic Opioid Usage

Case & Commentary—Part 1

A 42-year-old man with a history of asthma and chronic lower back pain was admitted to the hospital with community-acquired pneumonia and an asthma exacerbation. His primary care physician (PCP) had been prescribing high doses of long-acting morphine (MS Contin), oxycodone, and gabapentin for his low back pain. He was marginally housed and often slept in shelters.

On admission to the hospital, he was treated with nebulizers, antibiotics, and prednisone. Due to some odd behavior and suspicion for substance abuse, a urine toxicology test was sent on admission and was positive for benzodiazepines, methadone, and opiates. As neither the benzodiazepines nor the methadone were prescribed medications, the hospitalist confronted the patient who admitted selling his prescribed opiates and buying diazepam and methadone on the street. He stated that they could "control [my] pain better."

The patient in this case was prescribed opioids for his low back pain. Opioids are frequently and increasingly used in managing chronic non-cancer pain. In fact, data on sales and distribution of opioids per person, per year, show an increase from 96 mg of morphine equivalents in the United States in 1997 to 710 mg in 2010—enough to supply every adult American with 5 mg of hydrocodone 3 times daily for more than 45 days.(1,2) Furthermore, US patients consume an incredible 99% of all hydrocodone and 83% of all oxycodone worldwide.(1,3,4)

Unfortunately, the dramatic rise in use of therapeutic opioids is not based on evidence of their long-term efficacy or supported by safety data in the treatment of chronic non-cancer pain.(1,5-11) Many experts agree that the massive increase in prescribing is founded on extensive misconceptions and not based on evidence or proven safety.(1,2,5-7,10-12)

The increased prescribing of opioids to treat non-cancer pain has been widespread. In one of the earliest surveys, opioid prescribing for chronic pain in the ambulatory setting doubled from 8% in 1980 to 16% in 2000.(13) In a study from 2000 to 2005, the proportion of enrollees receiving opioids for chronic non-cancer pain grew 58% in the health insurance group and 29% in Medicaid.(14) By 2005, long-term opioid therapy was being prescribed to an estimated 10 million US adults.(1,2,15-17) Deyo and colleagues (3) showed that approximately 20% of patients in primary care settings were longtime opioid users; nearly two-thirds had received at least one course of opioids. In pain management settings, more than 90% of patients were receiving opioids on a long-term basis before presenting to interventional pain management settings.(18)

Most of this increased use likely relates to well-meaning efforts by clinicians to treat the often frustrating problem of chronic pain, as in this case. We do not have enough detail to determine whether this was necessary or appropriate. Yet, it seems from the case that the patient may have been using his prescribed opioids for non-medical purposes, which opens a window to a different side of the opiate safety problem.

Information on nonmedical use of opioids in patients with chronic non-cancer pain is not easily obtained. Nonmedical use, defined as use without prescription or outside the limits of prescription, occurs in 5% to 41% of patients.(19) Consequently, the overuse and abuse of opioids, including the escalation of the therapeutic use of opioids, can result in injury and death.(1,19) It is well known that high doses of opioids as well as the combination of multiple opioids, illicit drugs, benzodiazepines, and hypnotics may cause serious adverse effects including death.(1,19)

In 2012, the Centers for Disease Control and Prevention (CDC) (2) described the characteristics of patients who had overdosed on prescription medications and specifically reported the doses of opioids prescribed and the nature of the prescribing. Approximately 80% of the patients that were prescribed low doses (defined as less than 100 mg of morphine-equivalent dose per day by a single practitioner) accounted for an estimated 20% of all prescription overdoses. In contrast, among the remaining 20% of overdose patients, the 10% prescribed high doses (greater than 100 mg of morphine-equivalent dose per day) by a single prescriber accounted for an estimated 40% of prescription opioid overdoses.(1) The remaining 10% of patients seeing multiple doctors and typically involved in diversion of drugs for recreational purposes contributed to 40% overdoses.

The patient described here was on high doses of two different opioids, both long-acting morphine and short-acting oxycodone, which placed him at high risk for an adverse event. When prescribed in high doses, opioids are associated with an increased risk for overdose (in addition to having other adverse effects). Studies show that the majority of patients treated with traditional opioids experienced gastrointestinal- or central nervous system–related adverse events, the most common of which were constipation, nausea, and somnolence, often leading to discontinuation of opioid therapy.(1,19) Long-

term opioid therapy also leads to hormonal, central nervous, respiratory, and cardiovascular complications along with tolerance, dependence, and addiction.(1,19)

Providers may make multiple errors when prescribing opioids for non-cancer pain. We find it useful to classify opioid prescribing errors into four categories: (i) inadequate screening for safe and effective opioid use, (ii) inability to monitor adherence, (iii) improper selection of opioids, and (iv) insufficient consideration of comorbid conditions.

For the patient in this scenario, there may have been inadequate screening for safe use, potentially improper selection of opioids, and possibly insufficient consideration of his asthma. The patient was receiving high-dose long-acting morphine in addition to oxycodone for so-called breakthrough pain. Breakthrough pain may be a reality in cancer pain, but is generally not a part of non-cancer pain.(1) When a patient is prescribed long-acting opioids while continuing to take short-acting opioids, this can be a setup for fatality and death, particularly when comorbid factors are not taken into consideration.

Case & Commentary—Part 2

Given the complexity of the pain regimen and the diversion, the hospital's pain service was consulted. They changed his medications to methadone, hydromorphone, clonazepam, and venlafaxine. The morphine and oxycodone were discontinued. With this regimen, the patient had reasonable pain relief at the time of discharge. He was discharged with a prescription for a 2-week supply of medications and had a follow-up appointment with his PCP 10 days after discharge. Unfortunately, as it was a weekend the discharging hospitalist was not able to speak directly with the PCP but sent her an e-mail with the medication changes.

Five days after discharge, the patient was found unconscious at a subway station and pronounced dead at a local hospital following unsuccessful resuscitation. Based on the clinical presentation and details at the scene, the cause of death was likely from unintentional opiate/benzodiazepine overdose.

In reviewing his medications, the patient had refilled his long-acting morphine and oxycodone 1 day before admission. Unfortunately, this information was not available to the discharging hospitalist, and the patient stated that he had not gotten any recent refills of his opiates. The patient filled the new prescription for methadone, hydromorphone, and clonazepam on the day of discharge.

It is unclear from the case details whether the patient's unexpected death could have been prevented, but the scenario acts as a powerful reminder of the risks of opioid prescribing. Much can be done to prevent such events in the future. All providers should follow appropriate guidelines to provide proper prescriptions. Enhancing and updating clinical teaching and training is crucial for all providers, especially those involved in the areas of pain management. It has been suggested that pain management education for health professionals has been and continues to be insufficient. Consequently, a more comprehensive and contemporary curriculum for prescribers seems warranted.

Best practices for preventing errors and adverse outcomes when prescribing opioids are described in Figure 1. The algorithm involves a 10-step process with diagnosis, determination of medical necessity, establishment of treatment goals, informed consent, adherence monitoring, and addressing adverse effects, followed by continuation or discontinuation of opioids after initial treatment of 8 to 12 weeks.(20)

In the present case discussion, appropriate prescription practices unfortunately were not followed. The first error was prescribing both long-acting morphine and oxycodone in a patient with comorbid respiratory disorders, and who was marginally housed and lacked support systems. It might have been

more appropriate to start with a single short-acting agent to determine adherence and tolerance. The second issue refers to the hospitalist suddenly switching the patient to methadone even though the patient admitted to selling opioids and purchasing diazepam and methadone. Methadone is associated with significant variations in metabolism and cardiac toxicity including death. It would have been safer to manage with short-acting oxycodone. The combination of multiple drugs along with comorbid conditions and social instability should have been red flags.

Although screening for abuse of prescription opioids is common, there is limited evidence due to the lack of high-quality studies for the reliability and accuracy of available screening instruments. Furthermore, given the lack of long-term published quality literature, there is little evidence that screening for opioid abuse by any of the instruments will prevent abuse.(1) Prescription drug monitoring programs (statewide electronic databases) that collect data on substances dispensed in the states may help reduce risks in opioid prescribing. There is good evidence that prescription drug monitoring programs provide data on patterns of prescription drug usage, which may lead to earlier recognition of abuse. There is also fair evidence that prescription drug monitoring programs may decrease prescription drug abuse or doctor shopping.(1) However, there is only limited evidence that prescription drug monitoring programs reduce emergency room visits, drug overdoses, or deaths.(1)

Urine drug testing, as part of compliance monitoring, is crucial in managing opioid therapy. While patients may initially balk at this testing, urine drug screening for opioid misuse and abuse should be used as an exercise to strengthen the patient–physician relationship. Providers should clearly explain to patients that urine testing will build trust and allow for more effective prescribing of opioids. There is fair evidence for the diagnostic accuracy of urine drug testing and that it serves to identify patients who are noncompliant or abusing prescription or illicit drugs.(1) Moreover, there is good evidence that urine drug testing may decrease prescription drug abuse or illicit drug use when patients are in chronic pain management therapy.(1)

In the above case, inquiry of a prescription drug monitoring program including appropriate information from all the physicians and pharmacies involved could have prevented the dangerous prescription patterns. Thus, communication among health care professionals can be crucial. Urine drug testing may have helped identify some of the abuses.

Other steps can be taken to minimize the risk of harm in opioid prescribing. Pain clinics are indispensable; however, in this case the patient would have been best served with an addiction management program rather than pain clinic referral. The providers could also have engaged the patient in a formal treatment agreement (i.e., pain contract). Informed consent and a treatment agreement can be essential and should include clear descriptions of medication use and abuse, as well as consequences for violating the contract (Figure 2).

Stratification of risk for patients initiated or maintained on chronic opioid therapy is crucial to prevent misuse and abuse. Patients are generally classified as low risk, medium risk, or high risk. Patients with concurrent substance abuse and high risk for abusing the prescription opiates fall under the category of high risk. High-risk patients must be monitored frequently with repeat assessment in conjunction with prescription drug monitoring programs, random urine drug testing, and random pill counts. In addition, these patients should be placed on low-dose opioids (and not on combination opioid therapy) and should be weaned off opioids if they develop any aberrant behaviors.

This patient had significant abuse patterns and should have been considered as high risk, and, consequently, should never have been initiated on high-dose opioid therapy, should have been

appropriately monitored, and should have been weaned off opioids or referred to addiction management. This case provides a tragic lesson that can help us improve the state of opiate prescribing.

Take-Home Points

- The initial assessment in managing patients with chronic non-cancer pain should involve establishing the diagnosis, medical necessity, and treatment goals.
- The most common errors associated with opioid prescribing for non-cancer pain include the following: inadequate screening for safe and effective opioid use, inability to monitor adherence, improper selection of opioids, and insufficient consideration of comorbid conditions.
- Providers should ensure full informed consent before prescribing opioids and determine methods to monitor adherence.
- Patients who are prescribed opioids should be monitored continuously for adherence and adverse effects as well as screened for abuse; urine drug testing may be effective.
- Stratification of patients into low risk, medium risk, and high risk is an essential feature prior to embarking on initial treatment.

Anesthesia: A Weighty Issue

The Case

A 77-year-old woman was evaluated preoperatively in anticipation of an elective left hip arthroplasty. She reported having a history of hypertension that was reasonably well controlled on procardia, atenolol, and lisinopril. The patient reported no history of bleeding disorders, tobacco use, anesthetic complications, or other significant comorbidities. Her calculated body mass index was 34. She was medically cleared for surgery.

The following week, the patient underwent an uneventful left hip arthroplasty with general anesthesia via a laryngeal mask airway. She had stable vital signs throughout. She was breathing spontaneously following the procedure and was safely extubated and transferred to the recovery unit. The patient continued to receive doses of morphine sulfate for procedure-related pain, which became complicated by increasing somnolence. She was also noted to have oxygen desaturations and, as these persisted, an arterial blood gas was drawn that demonstrated an acidosis with a markedly elevated partial pressure of carbon dioxide ($PaCO_2$) of 81 mm Hg. Attempts at noninvasive ventilation failed and the patient was reintubated for hypercarbic respiratory failure. After better pain control and airway assessment, the patient was extubated the following day and had an uneventful hospital course to discharge. Providers suggested in the discharge summary that the patient likely had obstructive sleep apnea (OSA) and would benefit from formal outpatient testing. Given the reintubation in the recovery unit, the case was reviewed by the hospital quality committee and questions were raised whether obese patients undergoing anesthesia should receive formal preoperative screening for OSA.

Discharge Instructions in the PACU: Who Remembers?

The Case

A 42-year-old woman was diagnosed with a torn anterior cruciate ligament (ACL) in her left knee after a skiing accident. Before arthroscopic surgery, she had been given postoperative instructions for ACL repair, which included 50% weight bearing starting immediately. Upon examination of the knee under anesthesia and with visualization from the arthroscope, the surgeon determined that the ACL was only partially torn and that the joint had sufficient stability. Rather than ACL repair, the surgeon performed microfracture to address damage to the intraarticular cartilage as well as meniscus repair.

After the surgery, the surgeon briefed the patient in the post-anesthesia care unit (PACU) on his findings and the revised postoperative instructions. Because of the microfracture procedure, she was to be completely non-weight bearing for 6 weeks—a significant change from what had been originally anticipated. However, the patient was still groggy from the anesthesia and asked the doctor to give this information to her husband. The doctor called the number in the chart and made contact with the patient's mother-in-law who understood the surgeon to say that a second surgery would be required (rather than that a different type of surgery had been performed) and the patient should abide by the postoperative instructions he had given her. It was not understood by the mother-in-law that these instructions had in fact changed.

None of this was in writing. When the husband picked up the patient, the written discharge instructions from the surgeon were generic and personalized only with the handwritten phrase "do as instructed." Confused, the patient followed the original, now incorrect, postoperative instructions. The confusion was never discovered at two subsequent postop visits, in part because the surgeon never explained specifically how the rehabilitation guidelines had changed based on the new findings and change in plan during surgery. The patient pushed herself to bear weight several weeks after the surgery. When she experienced significant pain, she called the surgeon who then chastised her for not following the postoperative plan. Needless to say, the patient was upset and concerned that she may have harmed her chances for a full recovery.

Emergency Error

The Case

An 81-year-old woman with a history of pancreatitis presented with the acute onset of abdominal pain, nausea, and vomiting. On presentation, she was in distress due to severe abdominal pain. She was hypotensive and tachycardic. Based on the exam and initial imaging, there was concern for small bowel obstruction.

The decision was made to take the patient to emergency laparotomy. At the time of induction, she was given fentanyl, etomidate, and rocuronium. Almost immediately, her blood pressure dropped to 60/30 mm Hg. She was rapidly intubated, but her hypotension persisted despite epinephrine. Her heart rate slowed, and she ultimately developed asystole. Cardiopulmonary resuscitation was initiated. She received advanced cardiac life support for 10 minutes. She ultimately regained a pulse but required high doses of vasopressors to maintain her blood pressure. The operation was cancelled and she was taken to the intensive care unit. Over the next 12 hours she had progressive multi-organ system failure, and she died the following morning.

The hospital's case review committee felt the patient likely had severe acute pancreatitis and not a small bowel obstruction. The committee's judgment was that this represented a diagnostic error and that this was a preventable death (because surgery would not have been indicated in the management of her pancreatitis). The case raised many questions about the safety of and errors associated with emergency surgery.

Don't Use That Port: Insert a PICC

The Case

A 48-year-old woman receiving neoadjuvant therapy for breast cancer was admitted to the hospital with fever and abdominal pain. A computed tomography scan in the emergency department revealed acute appendicitis and surgery was recommended. Although the patient had a chest port in place, the surgeon refused to access the port, and instead requested placement of a peripherally inserted central catheter

(PICC). The surgeon believed that the port device should be exclusively used for chemotherapy, not to provide venous access for other purposes; he felt strongly that such use would increase the risk of infection. Although the vascular access nurse disagreed and advised that the port should be used for vascular access during surgery, the surgeon ordered PICC insertion by interventional radiology. The patient underwent a complicated PICC placement requiring multiple insertion attempts and adjustments. The next day, she developed severe arm pain and swelling and was found to have an acute deep venous thrombosis (DVT) involving the axillary and subclavian veins on the side of the PICC. Surgery was canceled, and she was placed on anticoagulation therapy and managed conservatively for appendicitis. The patient ultimately recovered but only after significant complications including contained perforation, peritonitis, and prolonged hospitalization (in addition to the blood clots).

Polypharmacy
The Case

A 65-year-old man with schizophrenia receives his routine outpatient psychiatric care through an agency. His case manager visits him weekly regarding medication adherence, which includes biweekly visits to his clinic for administration of his risperidone depot injection. He receives all his oral medications dispensed in weekly blister packs from his local pharmacy; however, the risperidone is provided by a separate "specialty pharmacy" that dispenses all long-acting injectable antipsychotics for the agency.

At his usual visit to his local pharmacy to obtain his oral medications, his pharmacist dispensed not only the usual oral medications but also the risperidone depot injection kit. The patient accepted the risperidone without disclosing this fact to his caregiver or case manager. On return to home, he reconstituted the powdered medication and self-administered the risperidone into his gluteus. Two days later, when contacted with a reminder regarding his upcoming injection (at the clinic), he reported his self-administration of the risperidone. The pharmacist at his local pharmacy was contacted and verified that the risperidone had been dispensed directly to the patient, even though it had never been previously filled by this pharmacy. This was a near miss, in that the patient did not receive the duplicate injection. The local pharmacy was advised to not dispense the injectable medication to the patient in the future.

Right Regimen, Wrong Cancer: Patient Catches Medical Error
Case & Commentary—Part 1

A 48-year-old man with a history of metastatic penile cancer was admitted to an inpatient internal medicine service for his fourth round of chemotherapy. He had three previous uncomplicated admissions where he received a standard protocol of 3 days of paclitaxel, ifosfamide, and cisplatin. The patient received this regimen for 3 days with minimal adverse effects. On hospital day 4, based on his previous admissions for chemotherapy, the patient was expecting to go home. In the morning his bedside nurse for the day came in and stated that she would be giving him his fourth day of chemotherapy. The patient was surprised by this and, before the chemotherapy was administered, asked to speak with the oncology team who was directing his care. After speaking with the patient, the oncology fellow examined the orders in more detail and realized that the incorrect chemotherapy regimen had been ordered for the patient. Rather than the 3-day regimen for metastatic penile cancer, the order set for a higher dose 5-day regimen of paclitaxel, ifosfamide, and cisplatin for germ cell cancer had been ordered. She and the attending oncologist discussed this with the patient and he was discharged later that day with no adverse consequences.

Oncology care is dangerous business. Patients with cancer have a potentially life threatening disease and often require toxic therapies for palliation or cure. Chemotherapy, a common treatment modality, requires expertise in all stages of the medication process as well as meticulous coordination of care. Oncology

team members of various specialties and professions (including physicians, nurses, pharmacists, and others) often work in different areas of a hospital or clinic, deliver asynchronous care, and follow complex treatment regimens. These regimens can involve multiple drugs administered in repetitive cycles, and are adjusted periodically to address toxicities. As the case illustrates, chemotherapy administration is among the more hazardous and challenging activities in all of medicine.

In light of the operational challenges of managing chemotherapy safely, there is surprisingly little epidemiologic evidence about the extent or nature of medical errors in chemotherapy care. In the Harvard Medical Practice Study, researchers examined medical records of 30,000 patients hospitalized in the state of New York in 1984 for medical errors and injuries. Only 3% of adverse drug events (ADEs) were attributed to "anti-tumor" medications, and these were generally deemed "unavoidable."(1) In a similar study of 15,000 patients hospitalized in Colorado and Utah in 1992, only 1.4% of ADEs were attributable to cancer chemotherapy, and none were judged to be errors.(2) However, in a seminal study of 4000 inpatients at two Boston hospitals, ADEs related to antineoplastic agents accounted for 7% of ADEs, but only 3% to 4% of medication errors.(3)

Several studies have focused specifically on chemotherapy errors in ambulatory settings, where the majority of cancer care is delivered. In a 2000 study conducted at a Boston cancer center, researchers examined more than 3200 chemotherapy orders for adult and pediatric patients. Errors were more common in drug ordering compared with administration or dispensing. The chemotherapy error rate was 3%, 2% of which had the potential to cause harm.(4) About half were intercepted by pharmacists and nurses, and no injuries occurred. Common chemotherapy-related errors included missed doses, "live" orders on days when clinicians decided to defer treatment, and failure to specify the blood counts and other laboratory test results needed to initiate therapy. In a more recent study of nearly 1400 adult and pediatric patient visits to four United States cancer centers or clinics, investigators reported chemotherapy error rates of 0.3 to 5.8 per 100 visits (depending on the site).(5) Errors most commonly occurred in administration (56%); having two concurrent sets of active orders was a particularly frequent source of error. In this scenario, one set of orders was written at the time of diagnosis and another, with adjusted doses, was written on the day of administration. A common theme in these studies is the relatively low error rate compared with non-chemotherapy medications, and the presence of errors related to redundant, confusing, or incompletely specified orders.

Two medication classes have attracted particular interest with respect to safe administration. Inadvertent intrathecal (into the cerebrospinal fluid) vincristine administration is nearly uniformly fatal as this agent is a potent neurotoxin. In a review of 41 such cases, adverse events were often related to the use of look-alike medication syringes and co-administration of intravenous and intrathecal therapy on the same day.(6) The risks associated with oral chemotherapy have also become better appreciated, especially as its use has become more common. Poor adherence, which reduces the chances of successful treatment, has been reported among selected populations with rates of 16% to 100%.(7) Common errors with oral chemotherapy involve dosing mishaps, sound-alike drug names, and supplying the wrong number of pills relative to the number of treatment days.(8) Taking a combination of pills of different strengths with interrupted daily or weekly treatment cycles can lead to confusion at home. Proposed solutions include the adoption of safe prescribing standards, a more meticulous approach to ensuring that patients and families are educated about the use and safe handling of these drugs, and developing better approaches for supporting adherence.(9)

In sum, there is limited data about the extent and nature of chemotherapy administration errors. The few published studies to date suggest that error rates are low, although these studies were performed in a small number of clinical settings. It is worth considering why chemotherapy error rates may be lower than error rates seen with other medications. Perhaps this reflects oncology clinicians' preoccupation with safe care,

given the vulnerability of the patient population and the inherent toxicity of chemotherapy. While cancer patients generally perceive chemotherapy care to be safe, they recognize that potentially serious harm could result from a mistake.(10) As illustrated in the case, another protective factor may be that many cancer patients are acute observers of their own care and able to partner with providers to identify and intercept errors before they cause harm.

Case & Commentary—Part 2

On formal review of the case, it was determined that the outpatient oncologist (a specialist in penile and germ cell cancers) had recommended the appropriate 3-day regimen to the oncology fellow. In this medical center, there was a functioning electronic health record (EHR) and computerized provider order entry (CPOE) system, but the chemotherapy order sets still existed on paper. In choosing the chemotherapy regimen, the oncology fellow inadvertently chose the wrong paper order set—he saw that the order set included the correct agents but failed to notice the higher dose and incorrect duration. The inpatient attending oncologist, who had not previously met the patient and was less familiar with penile cancer, co-signed the fellow's incorrect orders. Throughout the hospitalization, the primary internal medicine team copied and pasted the original oncology outpatient note that stated the patient would receive the 3-day course of chemotherapy, even though this differed from the 5-day regimen that was ordered. None of the other safety checks that existed (including the presence of a chemotherapy pharmacist and chemotherapy nurse checking the orders against allergies, renal function, body surface area, etc.) identified the dose and duration error.

In 2009, the American Society of Clinical Oncology (ASCO) and the American Nursing Society co-published a comprehensive set of chemotherapy safety standards.(11,12) Chemotherapy administration was divided into seven discrete steps: review of clinical information and selection of a regimen; treatment planning and informed consent; ordering or prescribing; drug preparation; assessing treatment compliance; administration and monitoring; and response and toxicity monitoring (Table). Although the original focus was on outpatient administration of chemotherapy, it was soon recognized that patients receiving inpatient chemotherapy may be at increased risk of errors. In 2012, reflecting this concern, the standards were revised and updated with particular focus on the inpatient setting.(13,14)

The current case illustrates the potential risks of inpatient chemotherapy. A national trend, in place for more than a decade, has resulted in a shift in the setting in which chemotherapy is delivered.(15) Chemotherapy administration has gradually shifted to the outpatient setting based on growing expertise in chemotherapy administration, better management of adverse effects, availability of highly effective antiemetics, less toxic chemotherapeutic agents, and technologic advances allowing for ambulatory delivery of continuous infusions. Many regimens, including each of the agents used in this case, can be safely administered in the outpatient setting. Although the trend also reflects patient preference to avoid hospitalizations, it has come at a cost. Many hospitals have experienced a disintegration of their inpatient oncology services, with fewer dedicated nurses and pharmacists available to manage patients who require chemotherapy.(15) Dedicated oncology units staffed by medical oncologists have been replaced by teams of general internal medicine–trained hospitalist services. The lack of expertise and specialized experience certainly can increase the likelihood of errors. In addition, while most hospitals and clinics have or will soon implement sophisticated electronic health record and computerized provider order entry systems, the introduction of electronic chemotherapy order entry systems often lags behind the larger systems. Many versions of hybrid systems can result, for example, in some hospitals all medication orders except chemotherapy being electronic; in others, ambulatory chemotherapy is ordered using an electronic system, but inpatient chemotherapy is ordered using paper-based processes.

As is often discovered during a root cause analysis, the error in the current case reflected a series of process failures that resulted in ordering the wrong chemotherapy regimen.(16) Fortunately, an alert patient had the courage to speak up in time to mitigate the error. The initial error—pulling the wrong paper order set—went undetected by the outpatient oncologist, the inpatient attending (who co-signed the incorrect order set), the inpatient chemotherapy nurse, and the chemotherapy pharmacist. The Figure is an example of an Ishikawa Diagram that identifies major categories that contributed to the failure; it is based only on the data provided in this case (in practice, an Ishikawa Diagram is created during a root cause analysis in which those involved in the error identify all potential contributing factors). The failure to recognize that the wrong chemotherapy was ordered was likely a combination of several factors including multiple handoffs, lack of content expertise by the inpatient fellow and inpatient oncology attending, insufficient supervision by the attending oncologist, and the location of the patient on a non-oncology unit. Finally, organizations that oversee inpatient care, such as The Joint Commission, have not specifically focused attention on the risks of chemotherapy administration. As a result, hospitals may not have invested the same financial and personnel resources to prevent errors in this arena that they may have spent in others.

The single most important step the hospital should take to prevent further inpatient chemotherapy administration errors is to understand the current process for ordering and administering inpatient chemotherapy. As is true for many health care–associated practices, it is likely that the process is unstructured, highly variable, and unreliable. Based on a reliability scale created by the Institute for Healthcare Improvement (IHI), processes that lack clear structures and protocols tend to rely on vigilance and hard work to prevent errors. Experts have described that such unstructured approaches at best achieve 10^{-1} reliability, a level at which 1–2 defects/10 opportunities is expected.(17) This would imply that if 10 patients a day at a given hospital are receiving chemotherapy, 1–2 per day may experience a medical error.

The first step toward improving the reliability of inpatient chemotherapy administration for this practice would be to standardize the process. This could entail a structured handoff between the outpatient and inpatient providers, a checklist to be shared by the inpatient oncologists, nurses, and pharmacists to ensure proper communication, and structured documentation. For example, a synoptic chemotherapy treatment plan has been advocated by the ASCO as a structured communication tool.(18) To achieve 10^{-2} reliability ($\leq$5 defects/100 opportunities) requires attention to human factors that contribute to failure in addition specific tools of improvement science. For example, a hierarchical organizational structure that discourages an employee from communicating concern can be improved by team training.(19) Finally, since the error also arose in part from a knowledge gap, it is not clear from the case that an electronic order entry system would have prevented the error.

The discovery of the error by the patient is notable and the team is to be commended for responding rapidly to prevent additional harm. This "intervention of last resort," though, cannot be depended upon. Not all patients are attentive, knowledgeable, and brave enough to voice concerns about their care.(20)

Take-Home Points

- In many hospitals, chemotherapy administration in the inpatient setting has become a "high-risk, low volume" procedure in which the risk of failure is high.
- The chemotherapy error occurred due to the lack of a high reliability framework and an over-reliance on vigilance and thoroughness.
- An electronic order entry system would not necessarily have prevented the error. Electronic solutions alone cannot overcome process failures.

Acute Care Admission of the Behavioral Health Patient

The Case

A 25-year-old man presented to the emergency department (ED) with a 3-week history of abdominal pain, nausea and vomiting, and weakness. His medical history included Crohn disease with ileocolectomy and ileostomy; chronic pain; schizophrenia and major depression with prior suicide attempts; and narcotic abuse with hydrocodone. Medications included mesalamine, clonidine, tramadol, haloperidol, olanzapine, venlafaxine, potassium chloride, and magnesium oxide. The patient was disabled, participated in an intensive case management program (ICM), and lived in supportive housing.

The ED work-up was consistent with acute pancreatitis and the patient was admitted to the hospital. A gastroenterology (GI) consult noted that olanzapine can cause pancreatitis. In addition, the GI consult described how the patient requested a reduction in the haloperidol dose because he felt overmedicated. The GI consult declined the patient's request and suggested that changes in the haloperidol dose, as well as the decision to discontinue olanzapine, should be made by the patient's psychiatrist.

Despite this advice, the medical team discontinued the olanzapine without consulting the patient's psychiatrist. The patient's condition improved and he was discharged to home. The discharge summary documented that the patient was instructed to follow up with his primary care provider, his gastroenterologist, and his psychiatrist in 1 week, and to inform his psychiatrist that olanzapine had been discontinued. Tragically, 2 weeks after discharge the patient committed suicide.

From Possible to Probable to Sure to Wrong—Premature Closure and Anchoring in a Complicated Case

The Case

A previously healthy 44-year-old man was admitted to the hospital with a 2-day history of headache and word-finding difficulties. Neurological examination was normal but computed tomography (CT) and magnetic resonance imaging (MRI) of the head revealed parietal and frontal masses concerning for malignancy or infection. Biopsy revealed evidence of vasculitis. Consultation with infectious disease, rheumatology, and neurology led to a provisional diagnosis of primary central nervous system (CNS) vasculitis. The patient was started on steroid and cyclophosphamide therapy and discharged after improvement in his symptoms.

Over the next month, the patient continued to feel well without a recurrence of his symptoms; however, serial brain MRI showed progression of the patient's lesions. Given his symptomatic improvement, the steroids were slowly tapered. A repeat MRI continued to show progression. Four months after the initial presentation, he re-presented to the emergency department after developing receptive and expressive aphasia and disorientation. Imaging again revealed evidence of worsening lesions and repeat biopsy showed glioblastoma multiforme. The patient underwent resection and adjuvant chemotherapy followed by rapid clinical decline.

Subsequent review of the case, including the clinical documentation, noted that the provisional diagnosis of CNS vasculitis at the time of hospital discharge gradually morphed into a certain diagnosis of CNS vasculitis during the ensuing outpatient follow-up, in both the minds of the clinicians and the chart documentation. As a result, the diagnosis was not revisited, even in the presence of contradictory data, leading to prolonged inappropriate therapy and a delay in the correct diagnosis and treatment.

Total Parenteral Nutrition, Multifarious Errors

Case & Commentary—Part 1

A 3-year-old boy on chronic total parenteral nutrition (TPN) due to multiple intestinal resections was admitted to an academic medical center for anemia. At baseline, the boy was developmentally appropriate but quite fragile medically, with multiple recent admissions for anemia and infections. Unable to take anything by mouth, he was completely dependent on the TPN for his nutrition and fluid intake, and had been so for more than a year. The boy had been doing well at home when he began having small amounts of bloody output from his ostomy site. His mother (the patient's primary caretaker at home) brought him to the hospital and he was admitted for further evaluation of the anemia. At the time of admission he was continued on his home TPN regimen.

The patient described in this case was receiving parenteral nutrition (PN), a life-sustaining therapy for individuals who cannot maintain or improve their nutrition status through the oral/enteral route. Such therapy is used in patients of all ages and across care settings (from intensive care units to the home). More than 350,000 hospital stays per year include PN, and tens of thousands of patients continue PN use at home.(1) During growth and development, PN is particularly important for children even when the PN solution does not provide the total nutrient needs of a patient. Anticipated adverse effects of PN include complications associated with intravenous access (e.g., thrombosis, bloodstream infection) and metabolic homeostasis (e.g., hyper- or hypoglycemia, fluid and electrolyte disorders). The risks associated with PN were addressed at a recent safety summit.(2)

High-Alert Medication, Complicated Process

What may be less well recognized is that PN has been characterized as a high-alert medication.(3) High-alert medications, by definition, are those that involve risk for significant harm when used in error. As such, safeguards are required to minimize error risk from PN. Notably, a patient's daily PN admixture may contain at least 40 active ingredients, each with dosing implications and interaction potential.

Even though the ingredients in PN may carry some risk, errors in the PN-use process may lead to even more safety hazards. The PN-use process refers to the numerous steps in providing PN therapy, including prescribing, order review, preparation (compounding) and labeling, dispensing, administration, monitoring, as well as ongoing patient assessment and documentation of each step.(1) These steps also involve numerous clinicians and caregivers from several departments, if not more than one organization or facility. Without a standardized process and full collaboration, many opportunities for error arise.(4) Although errors are known to occur, a limited number of publications discuss them. Such errors may easily result in PN ranking among the top causes of medication error, but very few organizations capture these or share them internally.(5) Moreover, unlike other high-risk medications, such as insulin or anticoagulants, limited literature describes the errors associated with PN use. A lone prospective observational study at one institution identified 74 PN-related medication errors (16 per 1000 PN prescriptions), with most occurring during transcription (39%), preparation (24%), and administration (35%).(4) Because this group had a nutrition support team that wrote the prescriptions, no PN ordering errors were identified that resulted in an incorrect admixture or subsequent patient harm. This structure is optimal but atypical, and mistakes in the PN prescription and in the PN order review process may contribute to additional harm and a significant number of errors not captured in this study. Nearly 10% of the errors identified resulted in or contributed to patient harm.(6)

Making PN Use Safer

In addition to standardization of the process and the expertise of those involved, the number of patients receiving PN is a critical factor. Most institutions manage fewer than 10 PN patients daily, and more than 80% manage 5 or fewer pediatric patients requiring PN.(5) Although this number may reflect appropriate PN use in favor of enteral nutrition when indicated, it also reveals the limited experience with PN in many

organizations. The expertise needed to safely manage patients requiring PN is analogous to the expertise expected in the drug-use process for cancer chemotherapy. Health care providers involved with PN should be knowledgeable and skilled in patient PN management and error prevention. Caregivers involved with PN should work within an interdisciplinary setting that includes certified nutrition support nurses, pharmacists, dietitians, and physicians.(7)

Despite being a complex and high-alert medication, only 58% of organizations have safeguards in place to prevent patient harm from errors in the PN-use process.(8) Approaches to improving the safety of PN can encounter significant organizational challenges but can be successful when based on published practice guidelines and standards.(9) To help organizations minimize errors when using use this complex therapy, practice guidelines and recommendations (based on evidence or generally accepted practices) are available from national organizations. The American Society for Parenteral & Enteral Nutrition (ASPEN) published the safe PN practice guidelines (10), but surveys have found that these guidelines have poor adherence.(5,11,12) Meaningful reductions in error rates have been reported in a pediatric setting that adopted a standardized PN process.(13) A revision of the 2004 ASPEN document is under way to provide graded, evidence-based clinical guidelines and a set of specific, actionable practice recommendations based on expert consensus.(5)

Transitions in Care and PN

Transitions in care create the opportunity for medication-related errors, which is certainly true for PN. One major contributing factor is the lack of prescription uniformity between institutions and across patient care settings; this variation is unmatched by any other medication in clinical practice. Myriad methods of ordering and labeling these complex PN preparations can be found. For example, varied units-of-measure can cause significant errors especially during transitions between hospital and home (14), at the least, errors involving the dosing of one or more of the dozens of active ingredients. Misinterpreted information from a PN label has led to error and patient harm in the transition from home to hospital.(10)

Ideally, one would hope the hospital described in the above scenario manages a high volume of patients on PN and adheres to the recognized national guidelines.(10) Their staff members should be well-trained in all steps of the PN-use process, and the hospital should have a standardized process to reduce the risk for errors.

Case & Commentary—Part 2

On hospital day 2, the patient's serum sodium was noted by the team to be low at 130 mEq/L (normal 135–145 mEq/L). The team ordered to increase the amount of sodium in the TPN from 5.2 mEq/kg/day to 5.5 mEq/kg/day based on a standard formula. The new TPN with the increased sodium began infusing at 9:00 PM. Overnight, the boy complained of worsening abdominal pain, which was treated with increased doses of intravenous opiates. He also complained of headache (which he never had previously, per the mother) and was irritable and could not be consoled. In the morning, his labs were notable for serum sodium of 158 mEq/L, which was confirmed on recheck. At first, the acute hypernatremia was attributed to dehydration. On rounds, the resident caring for the patient examined the TPN bag to see how much sodium the boy was receiving. The TPN bag had a sodium concentration of 55 mEq/kg/day (a 10-fold increase of the intended sodium concentration of 5.5 mEq/kg/day). The TPN was immediately stopped and the boy was given free water intravenously to correct the severe hypernatremia. Correction took more than 48 hours. Fortunately, the boy did not experience any adverse consequences from the hypernatremia.

On formal review of the case, multiple errors led to the excess sodium infusion. This academic medical center had a functioning electronic health record (EHR) and computerized provider order entry (CPOE) system. However, due to the complexity of TPN orders, they were completed by hand and then scanned to the pharmacy to be entered by the pharmacist into the CPOE system. The order for the increased sodium was written appropriately on the paper order, which was scanned to the pharmacy. The pharmacist (who was specifically trained to enter TPN orders) inadvertently entered 55 mEq/kg/day into the computer. A second pharmacist (also trained in TPN) reviewed the order by standard protocol and did not catch the dosing error. The order was then sent to the contracted pharmacy that prepared the TPN for this hospital, and there an additional two TPN pharmacists did not recognize the error. Automatic warning flags popped up in the system regarding the high sodium dose but these were ignored and dismissed as this boy had more than 8 warnings each day for his TPN order, even when entered correctly.

Speaking with the pharmacists revealed that there was not only an error in transcription but they also had incorrectly perceived 55 mEq/kg/day as 55 mEq/L/day, an appropriate dose for an adult TPN order. Because of this, the TPN order was produced with the high sodium concentration and sent to the hospital. Two nurses verified the TPN order was accurate and appropriate at the bedside and also did not notice the error.

The error in this case involved a breakdown in oversight and system checks; breakdowns leading to medication errors is a familiar scenario.(14) PN-related dysnatremia may be an all too common—though infrequently documented—error. As occurred in this case, multiple failures across the PN-use process are usually identified in retrospect as contributing to such errors. These can involve order entry and transcription errors, inappropriate abbreviations, dose designations or units-of-measure, PN component mix-ups (a bigger concern with ongoing shortages of many of these components), no warnings for catastrophic dose limits, catheter misconnections, and ineffective or nonexistent systems of independent double-checks.(14) However, as happened here, the issue often begins with PN prescription.

A broad survey of institutions revealed that only 32.7% use a computerized order entry system (CPOE) system for PN.(5) Even when CPOE is used for other medications, PN is seldom included. As in this case, most institutions still use handwritten orders requiring one or more error-prone transcription steps in the process. Available electronic health record (EHR) systems do not perform well when it comes to PN.(16) Current CPOE systems need significant improvement in nutrition support content including decision support tools. Such tools would allow for real-time alerts to any macronutrient or micronutrient dosing below or above accepted values.(5,16) Despite a number of obvious advantages over paper charts and handwritten orders, including the need for less order clarification or intervention, CPOE is of limited benefit if not built, customized, and subsequently optimized for all the users including those involved with PN.(12,17) Significantly less order clarification/intervention is required when using an electronic system compared with handwritten.(12,17)

Fully integrating a CPOE system with pharmacy system can help prevent PN-related errors. Without such integration, PN should be prescribed using a standardized order template as an editable electronic document to avoid any handwritten orders (Figure). The need for any calculations or data conversion should also be avoided. Although unthinkable for most other medications, the need to specify the dose of each macronutrient and micronutrient to be included in the PN admixture varies considerably between institutions; mixed methods (mg/L for some contents, mg/kg/d for others) are sometimes even used within an institution.(4) Due to the need for weight-based dosing of nearly everything, the use of mixed methods is more likely with pediatric patients. For example, electrolytes may be ordered either by salt or by ion, as well as varying units-of-measure (e.g., mEq or mmol per kg, per L, per day, or per total volume). The ordering process should include built-in decision support and alerts for when weight-based, population-specific dosing is out of range. In the absence of built-in decision support, the critical step of pharmacist

review becomes paramount. In the present case, the need to specify the dose in mg/kg/day and the need to transfer the order from a paper form to the CPOE system contributed to the error.

A survey found that 23.1% of organizations do not dedicate pharmacist time to review and clarify these orders.(5) The pharmacist should not only be trained to enter a PN order, but should be specifically knowledgeable in performing both a clinical review (e.g., dosing) and a pharmaceutical review (e.g., compatibility) of each PN order daily. Pharmacist interventions for all prescribing errors should then be documented in the permanent record. When knowledgeable pharmacists are involved, pediatric PN prescribing errors are identified and resolved at frequencies similar to those with other complex medications.(17)

Fewer than 10% of institutions have an interfaced electronic system for seamless transfer of a PN order from prescriber to pharmacy and the automated compounding device (ACD) that mixes the PN.(5) Error rates for preparing complex admixtures (including PN) are 22% to 37% depending on method of preparation.(15) ACDs are designed with the ability to provide users with alerts for dosing errors, however many institutions do not make full or appropriate use of these. Several reported PN-specific cases resulted from failure to incorporate built-in dosing limits in the ACD.(15) These limits prevent inadvertent catastrophic electrolyte doses from being included in the preparation, but require the software to be appropriate for patient age and weight. In addition to optimizing the ACD, standard operating procedures should be in place to independently double-check every step in the preparation process.

Multiple warnings occurred daily with this patient's PN order, and ignoring them contributed to the error in this case. No warning flags should be ignored or dismissed no matter whether they appear each day; each should be recognized, clarified, and documented by the pharmacist. One PN-related fatality occurred when an infant received a 1000-fold excess of zinc because of a mix-up in units and another when an infant received a 60-fold overdose of sodium.(15,18) The mix-up of dosing nutrients per kg or per day in another pediatric case was identified during PN infusion but before any adverse effect occurred.(19) When not automated, a second pharmacist should be involved in evaluating the original order against what has been transcribed, prepared, and labeled for dispensing. Some have argued that institutions should use commercially available pre-made PN formulations (not mixed from scratch at the institution). Unfortunately, commercially available pre-made PN formulations are not safer in the absence of a standardized PN-use process.(20)

The final steps in the PN-use process are administration of PN and ongoing monitoring. In this case, the nurses checked the solution against the incorrectly entered order. Instead, nurses administering PN should independently check the label against the original order. If any of the ingredients listed on the label are out of sequence or have a different dose or units than the original order, then the process should stop for clarification back up the chain through the pharmacy to the prescriber. Patient safety is worth the time it takes to verify the order. It is the responsibility of the involved prescriber, pharmacist, nurse, and dietitian to recognize and report all PN-related medication errors—whether they reach the patient or not.

The use of a CPOE system with decision support that interfaces with the pharmacy computer system thereby averting a transcription step would have prevented this patient's PN error. In the absence of such a system, required documentation of the pharmacist's review to include comparing the dose of each component against an age-appropriate table of accepted values would have also made the error less likely. Furthermore, had the nurses checked the PN label against the original order, the error may have been caught at this late step in the PN-use process.

Take-Home Points

- PN is a high-alert medication requiring safety-focused policies, procedures, and systems.
- Institutions should incorporate all appropriate ASPEN clinical guidelines and best practices documents.
- Providers should take the opportunity to enhance patient safety and reduce PN-related medication errors by becoming directly involved in the oversight of this therapy.
- Institutions should collect and report all errors associated with PN internally and externally (through the ISMP Medication Errors Reporting Program); further information is available on the ASPEN Web site.
- Providers should document each step in the PN-use process so that any errors can be evaluated and corrective actions taken to improve the process.

Pathologic Mistake

The Case

A 32-year-old previously healthy woman experienced abdominal pain and bloating for 6 months. The discomfort worsened with eating. After losing 15 pounds in less than 2 months, she visited her primary care physician. Initial imaging showed enlarged abdominal lymph nodes as well as jejunal thickening and dilated ileum in the small bowel. A lymph node biopsy and partial small bowel resection was undertaken. Lymph node pathology was reported as "Castleman disease, of hyaline vascular type," while the small bowel biopsy was normal.

Castleman is a rare disease in which immune cells in the lymph nodes proliferate. It is not considered a cancer, but is treated by physicians who specialize in lymphomas. With this diagnosis, her primary physician appropriately referred her to the lymphoma clinic. Physical exam, laboratory tests, and repeat computed tomography (CT) scans were all consistent with the initial workup, and the specialist began making plans to administer chemotherapy for Castleman. Still, the lymphoma specialist was struck by a number of inconsistencies. The combination of the location and number of affected lymph nodes would have made this an extremely rare presentation of an already rare disease. Also, CT findings of jejunal thickening and a dilated ileum were atypical for this diagnosis.

Puzzled, the lymphoma specialist requested a second pathology opinion from a tertiary care center with expertise in Castleman disease. The review reported reactive lymph nodes with hyalinization but no other features of Castleman, and normal small bowel. Plans for chemotherapy were cancelled. Lacking a diagnosis, further work-up was initiated. Upper gastrointestinal endoscopy and blood work was consistent with adult-onset celiac disease. She was started on a gluten-free diet. Follow-up imaging at 4 months showed dramatic improvement, and with strict adherence to her diet, the patient is still symptom-free.

The Unfamiliar Catheter

The Case

A 28-year-old woman, 20 months post–bilateral lung transplant, presented to the emergency department with sudden onset of severe shortness of breath and was admitted to the hospital. Diagnostic studies revealed that she was producing donor-specific antibodies. A large bore central line, similar to a hemodialysis catheter, was placed in her right chest, and daily bedside plasmapheresis therapy was initiated as treatment for humeral rejection.

A registered nurse (RN) received orders to draw the patient's morning labs. Although she had worked with many other types of catheters, the RN asked the charge nurse for instructions because she had no previous experience with this type of catheter. The charge nurse provided the RN with the following basic

verbal instructions: waste 3 cc, draw labs, flush with saline, HEP-LOCK. The RN felt confident that the verbal instructions were sufficient.

The patient was awake and in no apparent distress when the RN entered her room. The two chatted as the RN drew the patient's labs. After all the tubes had been filled the patient sat upright and said, "Something isn't right." As the RN reached around the bedside table to grab the saline flush, the patient began to convulse. The RN called for help as the patient lost consciousness and fell, bleeding from her catheter, to the floor. The patient spent the next 3 days in the intensive care unit (ICU). She was conscious yet unable to respond for the first 24 hours. Testing revealed a cerebral air embolism, and the medical opinion was that damage was likely to be temporary.

The nurse manager conducted an immediate and thorough incident review, which revealed that the RN had failed to clamp the catheter prior to removing the syringe, thus allowing air to enter the catheter and obstruct the patient's circulatory system. The devastated RN requested a temporary leave of absence, but never returned to work. The hospital enacted a policy allowing only trained RNs to access the catheters and requiring all RNs to receive mandatory education.

A Weighty Mistake

The Case

A 17-month-old toddler was brought to the emergency department (ED) by her parents with concerns about an infection around the eye. A triage nurse took the patient's vital signs, including her weight, and escorted her and the parents to a room for evaluation. The resident and attending physician diagnosed an uncomplicated periorbital cellulitis and prescribed clindamycin 225 mg orally three times daily based on the patient's weight. The patient received the first dose in the ED and was then discharged home.

The following evening, the patient's mother called the ED to report that the patient's discharge paperwork listed a weight of 25 kg rather than her true weight of 25 lb (11.3 kg). The mother, a medical student, realized the potential implications of such an error and asked the resident on duty to recalculate the appropriate dosage. The patient's dose was changed to 113 mg three times daily, and the patient continued the course with resolution of the cellulitis. Other than mild and self-limited diarrhea, there were no significant adverse effects from the four larger doses administered prior to the dose change. On further investigation, the initial triage nurse incorrectly entered the patient's weight (25 pounds) as a weight in kilograms in the electronic medical record (EMR), an error that was not caught by other providers throughout the ED visit.

CVC Placement: Speak Now or Do Not Use the Line

The Case

A 48-year-old woman with a history of hypertension, psychiatric illness, and a previous suicide attempt overdosed on her blood pressure medication (calcium channel blocker). When found unresponsive by her partner on the bathroom floor, she was brought by ambulance to the emergency department (ED). A right subclavian central line was placed during resuscitation.

No blood return was obtained from any of the lines. The ED team thought this was likely due to severe hypotension (her systolic blood pressure was around 50 mm Hg), but there was some concern that the line was not in the proper position. A chest radiograph was obtained when the patient arrived in the intensive care unit (ICU). The initial reading noted that the line might have been in the right atrium (which is to say, inserted too far). However, the radiology attending physician concluded the line was in good position.

Reassured, the line was used by the cardiology team to deliver medications and fluids during pacemaker insertion. Several hours later, a repeat chest radiograph was ordered after the patient began to vomit. This radiograph showed whiteout of the right lung, and ultimately the clinicians realized that the tip of the subclavian line was actually within the lung. Approximately 1400 cc of fluid was then removed from her pleural space via thoracentesis. Fortunately, the patient made a full recovery.

Death by PCA

The Case

A healthy 21-year-old pregnant woman delivered a healthy baby via Caesarean section after an uncomplicated pregnancy. Two hours after delivery, the post-anesthesia care unit (PACU) nurse removed the patient's epidural catheter (placed prior to Caesarean section) and implemented an order for a morphine patient-controlled analgesia (PCA) with a 2-mg bolus, 6-minute lockout, and a 4-hour limit of 30 mg. Two concentrations of morphine are normally available for PCA use, 1 mg/mL and 5 mg/mL. The nurse used a 5 mg/mL morphine cassette because a 1 mg/mL cassette was not available. Upon admission to the ward 3 hours after delivery, the ward nurse reviewed the history settings on the PCA pump and confirmed the pump settings were consistent with the order. However, she did not read the label on the cassette, open the pump, or assess the volume being infused.

Four hours after delivery, the patient complained of itching after breastfeeding her infant. The nurse administered 25 mg Benadryl intravenously followed by a second 25-mg dose of Benadryl 45 minutes later. Six hours after delivery the patient was alert, oriented, and awake. Later in the evening the patient was found asleep and snoring. Her vitals were within normal range and the nurse noted that 20 mg of morphine had been infused. Thirty minutes later the patient had no detectable pulse or respirations. Despite resuscitation efforts, she was pronounced dead 7.5 hours after initiation of the PCA.

Autopsy revealed a toxic concentration of morphine. The available evidence is consistent with a concentration programming error where morphine 1 mg/mL was entered in the infusion pump instead of 5 mg/mL.

Delay in Treatment: Failure to Contact Patient Leads to Significant Complications

The Case

A 21-year-old woman presented to the emergency department (ED) with heavy vaginal bleeding. She was admitted to the obstetrics and gynecology (OB/GYN) service for management. She received a blood transfusion and a Depo-Provera injection (a hormone to stop the bleeding), and was discharged home the next day. As part of the evaluation for her vaginal bleeding, a chlamydia test was performed in the ED. This test returned positive the day after the patient was discharged.

Per a standard protocol, the positive laboratory result was sent through the electronic medical record (EMR) to a nurse who worked in the OB/GYN clinic. She followed standard procedure and tried to call the patient using the contact number in the EMR. No one answered, and the nurse called again on each of the next 4 days, but there continued to be no answer. She notified her clinic supervisor who noted the result, but made no further attempts to contact the patient.

One week later, the patient presented to the radiology department for an ultrasound that had been scheduled at the time of the initial hospitalization. The ultrasound technician did not notice the abnormal test result or the fact that the chlamydia infection had not been treated. The following day, a different

OB/GYN clinic nurse tried to call the patient with the ultrasound results, and again no one answered the phone. She sent a letter by mail to the patient with both the ultrasound and chlamydia results. The patient received the letter and came to clinic 2 weeks later (now 26 days after her initial presentation) where she received appropriate antibiotics for the chlamydia infection (a single dose of azithromycin).

Despite this treatment, she developed fevers and abdominal pain and presented to the ED. She was diagnosed with chlamydial pyosalpinx (infection of the fallopian tubes) and peritonitis. This severe form of chlamydial infection likely developed because of the delay in treatment. The patient needed to be admitted to the hospital for intravenous antibiotics. The patient was discharged 3 days later and was expected to make a full recovery, although there is some risk of long-term complications including infertility and chronic pelvic pain.

Preventing PICC Complications: Whose Line Is It?

The Case

A 55-year-old woman with myasthenia gravis, hypertension, and hypothyroidism presented to the emergency department with 1 week of progressive left arm swelling, neck pain, and fevers. For the past year, the patient was receiving treatment for myasthenia gravis with intravenous immunoglobulin (IVIG) through a peripherally inserted central catheter (PICC). On admission, she was found to have extensive catheter-related thrombosis in the subclavian, axillary, and internal jugular veins. Her blood cultures subsequently grew *staphylococcus aureus* and she was diagnosed with endocarditis and osteomyelitis of her cervical spine. Her hospital course was complicated by sepsis, acute respiratory distress syndrome (ARDS), and multiorgan failure. The patient ultimately died during the hospitalization.

The hospital's quality committee reviewed the case. They noted that the patient had a PICC line placed at one facility but was receiving IVIG infusions at a different hospital closer to home. Questions were raised about who had responsibility for the line, whether it should have been replaced periodically to reduce infection risk, and what other strategies might have prevented this outcome.

A Real Heartache

The Case

A 60-year-old man presented to the emergency department (ED) with 2 hours of burning chest pain. The pain began at rest, and it radiated to his back and left axilla. He had no other complaints and reported being in good health otherwise. His past medical history was notable for a history of depression, a 40-pack/year history of cigarette smoking, and a father who had a heart attack at age 49. On physical examination, his initial blood pressure was elevated at 192/100 mm Hg, but his heart rate and the rest of his cardiopulmonary examination were normal. Bilateral upper-extremity blood pressures were equal. An electrocardiogram (ECG) was obtained (Figure 1) and interpreted as unremarkable. A chest radiograph and routine blood work, including a troponin assay, were also normal. The patient received aspirin and sublingual nitroglycerin without symptom improvement. Subsequently, a "GI cocktail" (an oral antacid/anesthetic combination) was given, and the patient reported symptom relief; his blood pressure also normalized. Convinced that a cardiac etiology had been ruled out because of the atypical pain, the unremarkable ECG, the normal troponin, and the response to the GI cocktail, the ED physician discharged the patient to home with a presumptive diagnosis of gastroesophageal reflux disease (GERD). The patient was advised to follow up with his primary care physician.

Two days later, the patient made an unscheduled return visit to the ED, now in severe distress. He complained of abdominal pain and was dyspneic, hypotensive, and with mottled skin. Fluid and pressor

support was initiated, and the patient was intubated. ED physicians obtained an ECG (Figure 2), which showed ST-segment elevation, prompting urgent cardiology consultation with concern for an acute myocardial infarction and/or aortic dissection. A bedside echocardiogram revealed a large pericardial effusion, and the patient was taken urgently to the cardiac catheterization lab. Cardiac catheterization showed branch occlusion of the left circumflex coronary artery. The patient stabilized and further evaluation did not reveal a myocardial rupture. Two days later, the patient had a cardiac arrest and could not be resuscitated. An autopsy revealed 3-vessel atherosclerotic coronary artery disease and a 4-day-old transmural myocardial infarct with extension and associated rupture of the left ventricular free wall. The consensus of the ED quality committee's case review was that the patient had a diagnosis of myocardial infarction, which was missed at his initial presentation.

The Lung Nodule That Refused To Grow

Case & Commentary—Part 1:

After moving to a new city, a 67-year-old man presented to a primary care physician for an initial visit to establish care. In discussing his past medical history, the patient described having a "spot" on his lungs that doctors had been following since 2004.

The solitary pulmonary nodule (SPN) can be defined as a single, well-circumscribed radiographic density measuring less than 3 cm, surrounded by aerated lung, and without any evidence of atelectasis, hilar enlargement, or pleural effusion.(1) Depending on the study population, between 15% and 75% of these nodules prove to be malignant.(2,3) The differential diagnosis includes malignant, infectious, inflammatory, and miscellaneous benign etiologies (Table 1).

In the past, most nodules were discovered incidentally on plain chest radiographs, as in this case. In recent years, it is more common for nodules to be identified by chest computed tomography (CT). However, nodules detected by CT often do not meet the classic definition of the SPN because either more than one nodule or an accompanying finding like atelectasis is present. Except for obviously calcified nodules (which can be attributed to old granulomatous disease), non-calcified nodules seen on chest radiography should be confirmed and better characterized by chest CT. CT characteristics associated with a benign etiology include smaller size, fat density, or a central, diffuse, or popcorn pattern of calcification. CT characteristics associated with malignancy include larger size, upper lobe location, irregular margins or spiculation, thick-walled cavitation, and hilar or mediastinal lymphadenopathy (Figures 1–3).

Patient-specific risk factors for malignancy include older age, current or former smoking status, prior history of extrathoracic malignancy, and asbestos exposure. Although most clinicians intuitively estimate the probability of malignancy, validated clinical prediction models can help refine decision-making. The Memorial Sloan-Kettering model calculates a patient's 10-year risk of developing lung cancer; although this model estimates risk before any radiographic imaging has been performed, it might be helpful in identifying patients in whom CT screening for lung cancer should be discussed.(4) Two other models—the Mayo Clinic model and the Veterans Affairs model—combine patient-level and radiographic characteristics to estimate the probability of malignancy for patients in whom a nodule has already been identified.(5,6) Based on a patient's probability for malignancy (low, intermediate, high), clinicians can use these models to choose an appropriate management strategy: monitoring with serial CT scans at designated intervals, performing functional imaging (e.g., positron emission tomography [PET]) to characterize the nodule further, or proceeding directly to biopsy (or even surgical resection) without further testing. The Mayo Clinic model has been validated in other populations and is widely used in practice to distinguish between nodules with a low risk of cancer (which can often be followed radiographically) and those with a high risk of cancer (which require tissue diagnosis and/or prompt resection).(7,8)

The most common avoidable error in the management of lung nodules is neglecting to review prior imaging studies. This can be essential in management; for example, if a solid nodule has been present for 2 or more years and has not changed, this is very strong presumptive evidence of a benign etiology, and no additional follow-up is required.(9) For sub-solid (ground glass) nodules, which are frequently premalignant or malignant but slow-growing, it may be necessary to demonstrate longer periods of stability to exclude malignancy.

The next most common error is to choose a strategy of "wait and watch" but neglect to "watch." This error ranges in severity from a minor delay in imaging (such as missing a single examination) to its most severe manifestation, in which the patient is lost to all follow-up either due to miscommunication or lapses in adherence. To date, robust electronic reminder systems for nodule evaluation have not been widely adopted, but there is a clear need for developing and testing these kinds of system-level solutions. Fortunately, the surveillance strategy is typically selected when the probability of cancer is very low or low, so this type of error infrequently results in harm.

Some might argue that it is an error to choose surveillance (as opposed to immediate intervention) for a nodule that ultimately proves to be cancerous. However, as long as this choice was the product of thoughtful deliberation that considered the risk of cancer and the benefits and harms of competing alternatives, we would characterize this as an undesirable outcome that resulted from an appropriate decision. Of note, there have been few systematic studies of outcomes following delayed diagnosis in patients with cancerous nodules, so the magnitude of harm associated with delay is highly uncertain.

Analogously, surgical resection of a benign nodule, although undesirable, may represent an appropriate course of action for a nodule that was considered likely to be malignant. In lung nodule evaluation, as in other areas of medicine, a bad outcome does not necessarily mean that an error was made.

However, it may be an error in judgment to select surveillance for a nodule that is likely to be cancerous, or to select surgical diagnosis for a nodule that is likely to be benign, highlighting the importance of accurately estimating the clinical probability of cancer. Such discordance should be infrequent, except for cases in which there are extenuating circumstances (e.g., strong patient preferences).

Case & Commentary—Part 2:

Upon further history, the patient stated that while undergoing hernia surgery in 2004, a nodule was seen on a routine chest radiograph. This had been followed up at the time with a CT scan and a PET scan. Based on these results, the nodule was felt to be benign and not an active malignancy or infection. The patient had no symptoms from the nodule.

After chest CT has been performed, there are four possible alternatives for the next step in nodule evaluation: PET scan, non-surgical biopsy, surgical diagnosis, or surveillance.

PET scans use 18-fluorodeoxyglucose (18-FDG) to measure the metabolic activity of a nodule. Although malignant cells are more metabolically active (and will therefore "light up" on a PET scan), infections and other types of inflammation (e.g., granulomatous) will also yield positive results, thereby compromising the specificity of the test. Smaller malignant nodules measuring less than 1 cm and sub-solid (ground glass) nodules can be missed by a PET scan.(10) The American College of Chest Physicians (ACCP) recommends PET for characterization of solid nodules measuring larger than 8 mm with a low to moderate probability for malignancy.(11) If PET shows increased uptake, this would prompt either biopsy or prompt resection. If PET shows no increased uptake, then watchful waiting with periodic surveillance is usually the preferred course.

Non-surgical biopsy is less invasive than surgical diagnosis and can be performed via transthoracic needle biopsy (TTNB) for peripheral lesions or bronchoscopy for central lesions. Endobronchial ultrasound (EBUS) and electromagnetic-guided navigational bronchoscopy (a computer program–aided navigational system for localizing lung nodules) increase the yield of bronchoscopic fine needle aspiration over routine bronchoscopy.(12) In addition, bronchoscopic procedures can simultaneously stage the mediastinal or hilar lymph nodes in the case of lung cancer.(13) For most nodules, CT-guided TTNB will have a higher yield than the newer guided bronchoscopic techniques, but it carries a higher risk of pneumothorax requiring chest tube placement (~7%).(14) At this point, the choice between these techniques will largely be based on the judgment and experience of the involved physicians, along with patient preference.

Surgical diagnosis, usually via a video-assisted thoracopic surgery (VATS), is often preferred for nodules that are very likely to be cancerous. The risk of a fatal complication from VATS wedge resection is low (

In the case under discussion, the nodule was "felt to be benign" based on the CT and PET results, suggesting that there was little or no FDG uptake on the PET scan. While this is reassuring, even a negative PET scan does not necessarily exclude the possibility of malignancy and additional follow-up is required, especially for sub-solid (ground glass) nodules. The optimal duration and frequency of surveillance is uncertain. For small (≤8 mm) solid nodules, most radiologists and pulmonologists defer to the expert consensus-based recommendations of the Fleischner Society (Table 2).(15) Although their recommendations are reasonable, it is important to note that they have not been prospectively validated. For larger (>8 mm) solid nodules, the ACCP recommends 3 rounds of surveillance (using non-contrast, low-dose techniques) at 3–6, 9–12, and 18–24 months.(11) For sub-solid (ground glass) nodules, a consensus is emerging that follow-up longer than 2 years is required to exclude slowly growing cancers, but the risks of extended duration surveillance (radiation exposure, workup of harmless incidental findings) should be weighed in relation to the putative benefits.

Case & Commentary—Part 3:

The patient had a 6-month follow-up CT scan in 2004 confirming the presence of the nodule and that it had not grown or changed in character. Subsequently, the patient had CT scans of the chest with and without contrast every 6–12 months for 8 years that showed no change in the size or character of the nodule. In total, he had more than 20 CT scans of the chest. The new primary care doctor wondered if all of the CT scans were necessary and how the nodule should have been managed.

Although the details of this case are murky, 8 years of follow-up is unquestionably excessive. Even for a sub-solid nodule, there is no evidence that follow-up of this duration is beneficial. Sub-solid nodules are usually identified by chest CT, and most are probably missed by chest radiography, so the nodule in this case was likely solid in appearance and perhaps even calcified. If benign calcification had been identified on the chest CT scan, then no additional follow-up would have been required. If the nodule was solid but non-calcified, as we suspect, then 2 years of radiographic stability is usually sufficient to exclude malignancy. While the harm caused by these additional CT scans is arguable, some studies have estimated that as few as 1 in 3000 patients scanned or as many as 1 in 300 patients scanned will develop cancer, depending on their age and sex.(16,17) Of course, there is also economic harm, with each scan costing several hundred, and in some settings, several thousand, dollars.

Take-Home Points

- Small pulmonary nodules (≤8 mm) are usually managed by CT surveillance.

    - For small solid nodules, the frequency and duration of surveillance are guided by recommendations from the Fleischner Society, which vary depending on the size of the nodule and the presence or absence of risk factors for cancer (Table 2).
    - For sub-solid nodules, which often represent low-grade cancers, the optimal frequency and duration of follow-up are highly uncertain, although there is an emerging consensus favoring extended duration follow-up in the range of 3 to 5 years.
- A systematic approach to evaluating larger (>8 mm), solid nodules includes the following steps:
    - Review old imaging studies.
    - Estimate the clinical probability of malignancy by considering both patient risk factors and nodule characteristics, or by using a validated prediction model.
    - Use functional imaging (typically with FDG-PET) to further characterize nodules when the clinical probability is low to moderate.
    - Provide information about the likelihood of cancer, the risks of procedures, and the potential benefits and harms associated with each of the alternatives for evaluation. Tailor the information about risk to the specific patient, when possible.
    - Elicit patient preferences for alternatives and outcomes (e.g., unnecessary surgery for a benign nodule versus delayed diagnosis and treatment of a malignant nodule). Help the patient make the best choice between CT surveillance, non-surgical biopsy, and surgical diagnosis.

Electrocardiogram Results: ***READ ME***
The Case

A 63-year-old woman with labile hypertension presented to the emergency department (ED) with new onset chest discomfort and an initial blood pressure of 210/100 mm/Hg. Her electrocardiogram (ECG) was unchanged from previous studies and her symptoms resolved with treatment of the hypertension. She was admitted overnight with orders for a morning ECG and serial troponin (ST) levels, the first of which was normal. At 6:00 AM, a nursing assistant obtained the ordered ECG and placed it in the patient's bedside chart without notifying a nurse or physician.

When the team was rounding 2 hours later, they reviewed the ECG, which was notable for new ST elevations inferiorly and laterally. The computer readout of the ECG stated, "****ACUTE MI****" and cited the ST elevations. On questioning the patient, she did report intermittent chest pressure overnight that was less severe than it was when she presented. Her morning troponin level also returned elevated, which was consistent with an acute myocardial infarction (MI). After urgent evaluation, she underwent successful coronary angiography and placement of two stents. She was discharged home without complications and on appropriate medical therapy.

The case raised concerns about the review of ECGs routinely performed in the hospital setting and often by those without the skills to interpret them. In this case, the nursing assistant later reported that she wasn't sure that "MI" meant "heart attack," but she also said that she doesn't routinely look at the computer interpretations. It was unclear whether the delay of 2 hours influenced the patient's outcome, but it could have.

Missed Pneumonia
The Case

A 32-year-old man presented to the emergency department (ED) with 3 days of fever and right pleuritic chest pain. Review of systems was negative for cough or dyspnea, and medical, surgical, and social history were unremarkable. The patient had taken a 2-hour plane ride the day before onset of symptoms.

On arrival to the ED, the patient was tachycardic at 106 beats per minute, tachypneic at 24 breaths per minute, and febrile to 38.8° C orally. No heart or lung abnormalities were noted on exam. Initial workup included a normal complete blood count (CBC) and basic metabolic panel (BMP), an elevated D-dimer (666 μg/mL), and a moderate right pleural effusion on chest radiograph. Although the clinicians had a high suspicion for pulmonary embolism (PE), a computed tomography angiogram (CTA) chest demonstrated moderate right pleural effusion without evidence of PE or infiltrate. The patient was discharged home with prescriptions for oxycodone/acetaminophen and ibuprofen. Discharge diagnoses were "fever, pleural effusion, and chest wall pain."

The patient returned to the ED 3 days later reporting worsening pain and continued fever with new cough and dyspnea. Examination was significant for tachycardia at 105 beats per minute, mild tachypnea at 20 breaths per minute, and diminished right-sided lung sounds. Laboratory test results, including CBC and BMP, were unremarkable. However, a chest radiograph now showed a right-sided effusion with consolidative changes, and a thoracentesis was consistent with parapneumonic effusion. The patient was started on antibiotics and admitted for pneumonia with effusion. The patient quickly improved on antibiotics and was discharged 2 days later.

Transfusion Overload
Case & Commentary—Part 1:

A 77-year-old woman with chronic myelodysplastic syndrome (a disorder of the bone marrow leading to chronic anemia) underwent an uncomplicated coronary artery bypass grafting procedure for coronary artery disease. Two months later, she presented to the hospital with shortness of breath and was found to have mild congestive heart failure (CHF). An echocardiogram revealed mildly reduced left ventricular function. She was given diuretics and discharged to a skilled nursing facility (SNF) for rehabilitation.

At the SNF, a follow-up complete blood count showed a hemoglobin level of 7.1 g/dL (normal 12–16 g/dL). Of note, her baseline hemoglobin was between 8 g/dL and 10 g/dL. At the time, the patient remained weak but had no new symptoms. She also had no evidence of gastrointestinal or other bleeding.

Her oncologist (who was managing the myelodysplastic syndrome) received the report the following day and arranged for the patient to be transferred to the emergency department (ED) for evaluation and transfusion. On arriving at the ED, the patient had no symptoms and normal vital signs. Her physical examination was unchanged from prior examinations and revealed no source of bleeding. A repeat hemoglobin level in the ED was 8.1 g/dL.

This case highlights the dilemma facing many clinicians caring for patients with anemia. What is the optimal hemoglobin threshold for red cell transfusion? For many decades, clinicians followed the "10/30" rule—that is, red cell transfusion should be utilized in order to keep the hemoglobin at 10 g/dL and hematocrit at 30%. The "10/30" rule, first recommended by Adams and Lundy in 1942 to improve outcomes in postoperative patients, was based on anecdotal evidence. Despite the lack of experimental evidence to support it, the "10/30" rule remained the standard for transfusion practices for more than 4 decades.(1)

In the 1980s, with the recognition that human immunodeficiency virus (HIV) could be spread through the blood supply, concerns grew about the risk of blood-borne infections. In 1988, the National Institute of Health Consensus Conference on Perioperative Red Blood Cell Transfusions concluded that "available evidence does not support the use of a single criterion for transfusion such as a hemoglobin concentration of less than 100 g/L [10 g/dL]."(2) However, the "right" hemoglobin concentration remained undefined.

The elderly patient in this case was found to have a hemoglobin concentration of 7.1 g/dL and 8.1 g/dL on repeat, which is at her baseline. The difference was likely not representative of a change but within range of lab variability for the same patient. She did not appear to be actively bleeding, and the anemia was likely due to her underlying chronic hematologic disorder. She was weak but otherwise had no new symptoms. Although anemia is associated with fatigue, generalized weakness, dizziness, and impaired exercise capacity, this patient did not appear to be acutely symptomatic from the anemia. Patients with clear symptoms related to anemia may benefit from transfusion, but it is not clear that she would have. In addition, while transfusion might transiently improve the patient's fatigue, her underlying myelodysplasia will likely lead to anemia again, and frequent transfusions could be required to prevent anemia. Transfusion in patients with chronic anemia is best avoided because of risks of iron overload and transmission of blood-borne infections. A better solution would be to use erythropoietin, which is effective in some patients with this disorder.

Notably, because this patient also has underlying cardiovascular disease, she may be less tolerant of anemia. In a study of 1958 surgical patients who refused transfusions due to religious reasons, there was a significant increase in 30-day mortality in patients with underlying cardiovascular disease compared with patients without cardiovascular disease when the hemoglobin dropped below 10 g/dL.(3) What has not been proven, however, is whether red cell transfusion reduces this mortality. In fact, in a recent trial in 2000 elderly patients with underlying cardiovascular disease or risk factors, patients transfused for hemoglobin levels of 10 g/dL experienced no apparent benefit when compared with those transfused at 8 g/dL or for symptoms.(4) There are no randomized clinical trials in patients with congestive heart failure (CHF) or in patients with chronic hematological disorders like myelodysplasia.

Given that this patient had no evidence of active bleeding, no clear symptoms related to the anemia, and the repeat hemoglobin in the ED was within her usual baseline range, there was no indication for a red cell transfusion. It would be reasonable to have the patient return to the nursing facility, continue rehabilitation, and recheck the hemoglobin level in 1–2 weeks.

Case & Commentary—Part 2:

The ED provider contacted the oncologist with the results of the evaluation, and the oncologist requested the patient be admitted to the hospital and transfused with 2 units of blood. He knew about her heart failure and stated that diuretics should be given between each of the units.

The patient was given the blood and the diuretics. Thirty minutes after the second unit of blood finished transfusing, the patient became lethargic and was found to have new hypoxia with an oxygen saturation of 60% on room air. She rapidly worsened and had a respiratory arrest; a code blue was called. She was successfully resuscitated and intubated and transferred to the intensive care unit (ICU).

A chest radiograph revealed vascular congestion and edema. The clinicians caring for her believed that the patient developed hypoxic respiratory failure from acute volume overload in the setting of CHF or from transfusion-related acute lung injury (TRALI; an immune-related transfusion reaction that leads to pulmonary infiltrates and hypoxia 0–6 hours after transfusion). A repeat hemoglobin level at the time was 11.7 g/dL. Because a normal response to a unit of blood is an increase in hemoglobin of 1.0 g/dL, the hemoglobin level of 8.1 g/dL might have been inaccurate.

With supportive care and more diuretics, the patient's hypoxic respiratory failure improved and she was extubated a day later. She remained in the hospital for 2 more weeks recovering from the episode and was transferred back to the SNF.

"Over-transfusion" can occur in the clinical setting where there is good-quality, randomized evidence to justify withholding red blood cell transfusion and a transfusion is given anyway. In our opinion, over-transfusion is common. Determining the incidence of over-transfusion is difficult because there have been few studies examining this, and they were conducted before the most recent evidence was made available. However, several studies have estimated the proportion of inappropriate transfusion at 24%–75%.(5)

Transfusion is not without risks.(6) Clinicians and patients are often most concerned about infections such as HIV and hepatitis. However, two of the more common serious adverse effects of transfusion are transfusion-associated circulatory overload (TACO) and transfusion-related acute lung injury (TRALI). The patient in this case presumably developed either TACO or TRALI, which occurs in 2 to 3 per 100 (7) and 8.1 per 100,000 transfused, respectively.(8) This particular patient had several risk factors associated with TACO: advanced age, underlying cardiovascular disease, and left ventricular dysfunction. Other risk factors that have been identified include transfusion rate and cumulative transfusion volume. A positive fluid balance, which may have occurred here, also places patients at risk for TRALI. Interestingly, pre-treatment with a diuretic has not been shown to protect patients from developing either of these potentially fatal consequences.(7,8)

For unknown reasons in the past, physicians had been taught to give 2 units of blood rather than 1 unit at a time. If this patient had been given 1 unit and then reassessed for the desired clinical response, as is recommended by all modern guidelines (6,9), the clinicians might have avoided giving the second unit, which seems to have led to respiratory arrest. This reassessment would have been especially prudent given this patient's left ventricular dysfunction.

The optimal transfusion threshold continues to be a subject of much debate, although two trials provide important data. The first study is the Transfusion Requirements in Critical Care (TRICC) trial. In this trial, 838 normovolemic ICU patients were randomized to either a "restrictive" or a "liberal" transfusion strategy.(10) Patients in the restrictive group were transfused if the hemoglobin dropped below 7 g/dL, and those in the liberal group received red cell transfusions for hemoglobin levels less than 10 g/dL. There was a trend toward lower 30-day mortality in the restrictive group (18.7% vs. 23.3%), and all other negative outcomes occurred less frequently in restrictive group.

The second, and most recent, trial is the Transfusion Trigger Trial for Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS).(4) This study randomized 2016 patients undergoing surgical repair for hip fracture with a history of cardiovascular disease, or with risk factors of cardiovascular disease, to a restrictive or liberal transfusion strategy. Those in the restrictive group received red cell transfusion only if the hemoglobin concentration was less than 8 g/dL, or if they developed symptoms of anemia. Patients in the liberal group were transfused to maintain a hemoglobin level greater than 10 g/dL. The primary outcome (being able to walk 10 feet or across the room at 60 days) was similar in both the liberal group (35.2%) and restrictive group (34.7%). The rates of in-hospital death or acute coronary syndrome were also not statistically significant between the liberal group (4.3%) and restrictive group (5.2%).

A recent meta-analysis examined 19 randomized, controlled studies that evaluated transfusion thresholds utilizing a restrictive or liberal transfusion strategy.(11) Using a restrictive transfusion strategy saved an average of 1.19 units of blood per patient transfused. Hemoglobin concentration was 1.5% lower in the patients allocated to a restrictive strategy. There was no difference in 30-day mortality or any other clinical outcomes between restrictive and liberal transfusion strategies.

Incorporating recent, emerging evidence and this systematic review, the AABB (formerly, the American Association of Blood Banks) published new guidelines on red blood cell transfusions in 2012.(6) In

stable, hospitalized patients, these guidelines recommend adhering to a restrictive transfusion strategy, with a transfusion threshold at a hemoglobin level of 7 g/dL (in ICU patients) and 8 g/dL (in surgical and medical patients). In patients with a prior history of cardiovascular disease, the AABB also recommends a restrictive transfusion strategy and states that transfusion should be considered at a hemoglobin level of 8 g/dL or less, or symptoms of anemia related to coronary artery disease (e.g., chest pain thought to be cardiac in origin, CHF symptoms, or unexplained tachycardia or hypotension unresponsive to fluid replacement). Due to a lack of evidence, the AABB could not recommend for or against a liberal or restrictive transfusion strategy in patients with the acute coronary syndromes (myocardial infarctions or unstable angina). We advise carefully assessing each patient for the need of transfusion. Finally, the AABB suggests that symptoms of anemia, as well as hemoglobin level, should also be factored in the decision to transfuse. It is important to emphasize that the hemoglobin concentration of 7–8 g/dL is recommended to *consider* transfusion. If the patient is stable, blood may not be needed.

We recommend using the AABB guidelines, which integrate the latest and best-quality evidence. Disseminating the guidelines requires an intense educational campaign to include all those who would be involved in making the decision to transfuse a patient—clinicians, nursing staff, blood bank personnel, and housestaff. A systematic review evaluated 19 studies that examined various behavioral interventions aimed at reducing blood product use.(12) The different interventions studied included individual/group education, guidelines, audit with feedback, audit with approval, or the implementation of a new form with criteria for transfusion. All of these methods were equally as effective in reducing either the amount of blood products transfused per patient (range, 9%–77%) or the proportion of patients transfused (range, 17%–79%). Similarly, a more recent study found that targeted education combined with a decision support intervention with computerized physician order entry decreased the percentage of inappropriate transfusions by 8.8%–13%.(13) In the end, specific interventions must be tailored to each institution's unique characteristics and provider and patient profile.

Ultimately, the decision of whether or not to transfuse a particular patient is complex. Each patient's unique clinical course and situation must be considered, and the risks versus the benefits of a red blood cell transfusion must be weighed. The evidence suggests that a restrictive transfusion strategy, utilizing a hemoglobin concentration of 7–8 g/dL (or symptoms of anemia) as a transfusion threshold, has been shown to be safe in most stable hospitalized, perioperative, and ICU patients, including those with underlying cardiovascular disease. The transfusion threshold for patients with acute coronary syndrome is unknown, and this area needs further research.

Buprenorphine and the Medically Ill Patient

The Case

A 60-year-old man with a 15-year history of oxycodone dependence presented to a substance abuse detoxification program with acute withdrawal symptoms, including dilated pupils, nausea, vomiting, diarrhea, and hot and cold flashes. He reported his last opiate intake was 2 days earlier. He felt his addiction was out of control and he wanted treatment.

His medical history was notable for hypertension and a 30-year history of tobacco use (2 packs per day). He went to a local emergency department (ED) a month ago for a cough. No outside medical or prescription records were obtained prior to initiating treatment. On physical examination, abnormal findings included dilated pupils, elevated heart rate and blood pressure, hyperactive bowel sounds, and scattered wheezes and rhonchi bilaterally.

Per the treatment program's protocol, the patient received buprenorphine/naloxone (4.0 mg/1.0 mg) for opiate detoxification, first at 2:00 PM and then again at 4:00 PM. When the nurse checked on the patient at 7:00 PM, he was difficult to arouse and cyanotic with notable respiratory muscle retractions, a respiratory rate of 8 breaths per minute, and oxygen saturation of 67%.

The patient was transported to the nearest ED where he was diagnosed with acute opiate-induced respiratory distress complicated by pneumonia and chronic obstructive pulmonary disease. The ED staff obtained outside medical and pharmacy records, which indicated the patient was hospitalized with community-acquired pneumonia and chronic obstructive pulmonary disease at another hospital 3 weeks prior and was given a prescription for oral antibiotics and other medications, which he never picked up from his pharmacy. Fortunately, the patient made a full recovery after 4 days on the medicine ward and was then discharged back to the substance abuse unit.

Looking for Meds in All the Wrong Places

The Case

A 40-year-old uninsured woman with anxiety ran out of her prescribed clonazepam and had a seizure. She went to the emergency department (ED) where she was given the prescription, but before the patient was discharged she had another seizure. The ED doctor saw the patient and made plans to discharge her after she received an intravenous (IV) administration of phenytoin (another antiseizure medication), assuming she was doing well and had stable vital signs.

The order was written correctly in the electronic medical record (EMR) for phenytoin, 800 mg IV. The drug-dispensing machines stocked phenytoin in 250 mg/1 mL vials. The correct dose therefore would require 4 vials and be equal to 3.2 mL to be added to a small IV bag. The nurse misread the order as 8000 mg (8 g) and proceeded to administer that dose to the patient, which was a 10-fold overdose and 2 to 3 times the lethal dose. The patient died several minutes after the infusion.

The error was noted during the code blue. The nurses responding to the code noticed the dozens of vials and the IV bag, which had a notation indicating the medication and the dose. An audit of the pharmacy system revealed that the nurse had taken 32 vials out of 3 different pharmacy dispensing machines to accumulate 8 g of IV phenytoin. Moreover, the nurse had to use two IV bags and a piggyback line to give that large a dose. Within 100 feet of the ED nurses' station were several ED doctors, a number of nurses, and a pharmacy with a PhD pharmacist on duty. The nurse did not ask anyone to check her calculations, nor did anyone notice or comment when she was moving around the unit amassing the vials needed for the dose.

CA-MRSA Skin Infections: An Ounce of Prevention is Worth a Pound of Cure

The Case

A 16-year-old adolescent boy was a member of his junior varsity wrestling team. One morning during wrestling season, he noticed a sore spot on his left buttock, assumed it was an insect bite, and applied hydrocortisone cream. Two days later, he noticed the bump was larger with a small amount of pus at the center. Assuming it was an ingrown hair, he expressed the pus. He attended school and practice the next day and did not mention the bump to his parents, teachers, or coach. It was his turn for "mat duty" after practice, and he used the same mop that was used every day to wipe down the mats. As the week progressed, he noticed the bump was increasingly tender and painful to sit on. After several days, the lesion had grown larger and was now red, raised, and warm, and he notified his mother.

His mother took him to the pediatrician that day. His vital signs were within normal range and he rated his pain 6/10. His pediatrician, who had seen him regularly since birth, noted that his immunizations were up to date and he had no chronic illnesses or prior hospitalizations. He had a history of a Septra allergy (trimethoprim-sulfamethoxazole), with a rash associated with past treatment of otitis media. The pediatrician ruled out brown recluse spider bite due to geography, and his wrestling made the pediatrician suspicious of community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) skin infection. The pediatrician incised the lesion, expressed pus, and cultured the fluid. Considering his Septra allergy, the pediatrician prescribed oral clindamycin 450 mg every 6 hours for 10 days, with follow-up in 7 days, and ibuprofen for pain.

Four days after starting antibiotics, the patient complained of hip pain with ambulation and he assumed he had pulled something during wrestling practice. He was observed to be pale and complained of chills and hip pain. His temperature was 102° F. His mother noted the lesion was larger and his whole buttock was red and swollen with red streaks. She immediately took her son to the emergency department (ED).

Deep tissue debridement of the hip lesion was performed in the intensive care unit (ICU) because the patient was not stable enough to have it performed in the operating room. Despite the debridement and appropriate antibiotics, by hospital day 3, he developed acute renal failure necessitating peritoneal dialysis and respiratory failure requiring intubation. Results from the original wound culture revealed CA-MRSA resistant to clindamycin. A radiograph showed extensive erosion at the femur head secondary to osteomyelitis.

The patient had a prolonged and stormy hospital course. On ICU day 20 he was extubated and moved to the step-down unit. As a result of the femur head destruction, he required a left total hip replacement. He continued physical therapy at home and was referred to a psychologist for long-term management of the issues surrounding his disability. It is expected that he will require hip replacements every 10 to 30 years for the rest of his life.

Undetected Foreign Object

The Case

A 75-year-old man with a past medical history of end-stage renal disease (on hemodialysis), hypertension, and diabetes was found to have obstructive, multi-vessel coronary artery disease. The patient was referred for bypass surgery and mitral valve repair. He underwent successful surgery and was discharged to a rehabilitation facility where he recuperated at the expected rate.

The patient continued to attend hemodialysis and clinic visits without fail. Eight months later, he was admitted to the hospital with shaking chills and confusion and found to have an empyema (i.e., collection of pus) on the left side of his chest. He underwent thoracic surgery where the trapped lung was freed from its adhesions and a 12-cm red-rubber snare was recovered—a surgical instrument from the prior surgery. The patient recovered to his baseline level of functioning after a 10-day intensive care unit (ICU) course followed by treatment in a rehabilitation facility.

On subsequent investigation, hospital staff members were puzzled by the failure to detect the object. The patient underwent three-times weekly dialysis sessions, at least eight clinic visits with multiple physicians, and had no symptoms until his dramatic presentation many months later. He also had seven chest radiographs postoperatively in which the device was not detected.

Empty Handoff

The Case

A 29-year-old man with "brittle diabetes" was admitted to the surgery service for incision and drainage of a leg wound. The patient's medical history included chronic renal failure, hypertension, and prior stroke after a hypoglycemia event. Prior to surgery while still on the hospital floor, the patient's blood glucose level fell precipitously after receiving insulin, requiring glucose several times. Due to workload, the nurse did not accompany the patient during transport to the operating room (OR). Instead, the nurse informed the transportation assistant about the patient's extreme sensitivity to insulin.

The transportation assistant neglected to pass this information on to the surgical nurse or the anesthesiologist. The electronic health record (EHR) did not reflect the glucose levels because the bedside glucose-monitoring device was not docked, so the information did not upload to the EHR for physician or nurse review. The patient spent 90 minutes in surgery and went to the recovery room where the blood sugar level was found to be 15 mg/dL, confirmed on repeat testing. Fortunately, the patient recovered quickly once he received intravenous glucose.

Peripheral IV in Too Long
Case & Commentary—Part 1:

A 75-year-old man with a history of coronary artery disease and congestive heart failure (CHF) was admitted to the hospital with a CHF exacerbation. He was given intravenous (IV) diuretics and improved over the first 4 days in the hospital. At this medical center, there was a standard protocol that called for all peripheral IV catheters to be replaced after 4 days to prevent infection. Because of edema in his extremities, placing a new peripheral IV was going to be difficult. The bedside nurse asked the covering physician if the peripheral IV could be extended for an additional day or two. The physician was planning on discharging the patient the next day, so the extension was approved.

There has been substantial focus on the risks associated with central venous catheters including catheter-related bloodstream infections. Yet, peripheral intravenous (IV) catheters are much more common in modern hospitals and also have associated risks. This case provides one example of the hazards of this seemingly benign medical device.

Peripheral IV catheters allow reliable and convenient delivery of life-saving medications for hospitalized patients. Placement of a peripheral IV catheter, however, is often a painful experience for patients. For staff with limited experience in placing peripheral IV catheters, multiple attempts may be required, especially for those with difficult venous access. So the decision to extend the peripheral IV catheter by the covering physician in the present case is perfectly understandable.

Nevertheless, peripheral IVs can be associated with multiple complications. Phlebitis (inflammation of the vein where the IV is placed) complicates IV therapy in 2.3%–60% of cases in different series.(1-3) The typical clinical presentation is pain and redness at the IV site. While most cases of phlebitis are noninfectious (just inflammation of the vein), this can progress to suppurative soft tissue infections (cellulitis, abscess, or tissue necrosis). Although rare (incidence rate: 0.06 cases per 1000 bed-days), this complication can cause serious morbidity.(4) Another serious complication is peripheral IV catheter–related bacteremia, which occurs in 0.1% cases (0.5 per 1000 IV catheter-day), although the frequency is lower than that of central line–associated bacteremia (4.4%, 2.7 per 1000 catheter-day).(1,5)

In an effort to decrease the risk of catheter-related infections, scheduled replacement of peripheral IV catheters every 48–72 hours or every 72–96 hours has been widely used.(3,6-8) Despite the popularity of this practice, there is no strong evidence supporting it.(3,7,9) Based on findings that rate of phlebitis is not significantly different between peripheral IV catheters left in place for 72 hours versus 96 hours (10), the

Centers for Disease Control and Prevention (CDC) recommends against replacing the peripheral IV catheter more frequently than every 72–96 hours.(6)

On the other hand, it should also be kept in mind that once peripheral IV catheter–related infectious complications do occur, infected catheters should be removed as soon as possible to prevent them from becoming a source of bloodstream infection. After inserting IV catheters, the site should be inspected daily, either at the time of changing dressing or by palpation through an intact dressing.(6,11) Erythema, tenderness, or other evidence of local inflammation should prompt the removal of the IV catheter.(6) In any case, it is imperative for the attending physician to inspect the IV catheter site to make sure that no early signs of phlebitis go unrecognized (4) before making the decision to extend the peripheral IV catheter.

In the case above, if the IV were functioning and the site lacked evidence of inflammation, it seems reasonable to extend the IV to 96 hours, particularly in light of the difficulty of placing a new IV and the potential pain to the patient.

Case & Commentary—Part 2:

The next day the patient was worse and required ongoing hospitalization. The peripheral IV was kept in place for 2 more days. On hospital day 6, the patient developed erythema around the IV site. With concerns for infection, the IV was removed and a new peripheral IV was placed. Later that day, the patient developed fever and chills. Blood cultures drawn at the time grew methicillin-resistant Staphylococcus aureus (MRSA), *most likely secondary to the infected peripheral IV catheter. Subsequently, the patient complained of back pain and a magnetic resonance imaging (MRI) of the spine revealed an epidural abscess, which on aspiration grew MRSA. He required 6 weeks of IV antibiotics for the MRSA bacteremia and epidural abscess. The patient ultimately recovered and was discharged to home.*

There is no mention whether the physician or the nurse inspected this patient's catheter site at 96 hours, but by 144 hours, cellulitis had developed at the catheter site. Sadly, the unexplained clinical deterioration of this patient—who was scheduled to be discharged—was likely caused by peripheral IV catheter infection. The local soft tissue infection led to MRSA bacteremia and then to an epidural abscess. Fortunately, after aggressive therapy and a prolonged course, the patient eventually recovered. The extra cost of MRI, imaging-guided aspiration of epidural abscesses, 6-week IV antimicrobial therapy, as well as the prolonged hospitalization, is likely to be in the hundreds of thousands of dollars, not to mention the patient dissatisfaction and potential for litigation. This case therefore highlights the serious costs—both clinical and economic—that can be associated with peripheral IV catheter infections.

Case & Commentary—Part 3:

In response to this event, the medical center involved developed a strict policy under which peripheral IVs must be changed every 3 days. They can be extended for 1 additional day with a physician's order but no longer. In addition, the medical center changed some of the nursing documentation to include the date of peripheral IV insertion and a description of the site during each shift.

It appears the medical center took some steps to try to prevent future peripheral IV infections. But, are these the highest-yield interventions? What should be learned from this case and what should be changed?

In this case, there were multiple issues with the IV management. The process of insertion was probably a difficult one in the presence of edema in the extremities, and staff with limited experience may have been

unable to maintain good aseptic technique. In addition, there was inadequate and delayed recognition of the catheter infection; by the time it was recognized on day 6, cellulitis and bloodstream infection had already developed. These may have been due to a lack of expertise in day-to-day management of IVs and IV sites.

Best Practices for Management of Peripheral IVs

There are system interventions that can help prevent IV catheter complications. A randomized controlled trial demonstrated that a dedicated IV therapy team of registered nurses specially trained for inserting IV catheters and inspecting catheter sites significantly reduced both local and bacteremic complications of peripheral IV catheters.(11) Moreover, a large prospective study of 3165 patients also showed that deployment of well-trained IV teams can effectively prevent peripheral IV catheter infection.(12)

The insertion site, method of insertion, catheter type, and maintenance protocol all seem to matter as well. In adults, upper extremities are the preferred site for catheter insertion.(6) Using an insertion site in lower extremity has been found to be an independent risk factor for catheter-related soft tissue infection.(4) For skin disinfection before the insertion of IV catheter, 2% alcoholic chlorhexidine is more effective than 10% povidone-iodine in the prevention of catheter-related infections.(13,14) Teflon or polyurethane catheters have fewer infectious complications than catheters made with polyvinyl chloride or polyethylene.(2,6) After placement of an IV catheter, the catheter site should be covered by either sterile gauze or a sterile transparent semipermeable dressing.(6,15) The use of a continuous infusion to maintain IV catheter patency is an independent risk factor for microbiologically-proven catheter infection (12) and catheter-related soft tissue infection.(4) The use of a closed intermittent infusion system with a plastic cap that can be cleansed before drug injection is safer. For IV catheters not used for infusion of blood product or lipid emulsions, the IV administration sets in continuous use, including secondary sets and add-on devices, should be changed no more frequently than every 96 hours, but at least every 7 days.(6,16) Adoption of the above-stated simple, inexpensive, and evidence-based practices is the best approach to prevent similar events in the future.

All of this brings us back to where we began: What is the optimal frequency to change peripheral IV catheters? As described above, there is no strong evidence in support of routinely changing catheters at 72 hours. We do know that longer (greater than 48 hours) catheter dwelling time is a risk factor for phlebitis.(1,2) In a prospective study of 3165 patients, however, the majority of phlebitis cases were culture-negative, suggesting the local inflammation was not caused by infection, and that extending the scheduled catheter replacement interval from 48–72 hours to 72–96 hours did not significantly increase the risk of microbiologically proven catheter infection.(12) A recent Cochrane review found no conclusive evidence of benefit in changing IV catheters every 72–96 hours in comparison with clinically indicated replacement in terms of the rates of IV catheter–related complications.(3,7,17) However, the two clinical trials reviewed were statistically underpowered for examining whether the risk of catheter-related bacteremia increases in clinically indicated replacement group.(6,10) A longer replacement schedule or clinical indicated replacement strategy has benefits in patient comfort and cost-savings, which need to be weighed against the potential harm of increased risk of catheter infection, especially bacteremia. In the absence of well-trained IV teams, replacement only when clinically indicated carries the risk of delayed recognition of catheter infection by inexperienced staff, until the development of serious consequences, as illustrated in the present case. In adult patients, replacement of peripheral IV catheters at 72–96 hour intervals is more comfortable for patients as well as less expensive than routine 48–72 hours exchanges, without significant increase in infection risk.(6)

The medical center attributed this adverse event to nonadherence to standard operating procedure, and in response, strictly enforced a scheduled replacement of peripheral IV catheters every 72–96 hours, which

is consistent with the CDC recommendations.(6) This straightforward solution, although commendable, may not be enough to prevent future events. Efforts should be directed toward enhancing expertise in IV catheter insertion and maintenance, rather than focusing on the replacement schedule.(12) To ensure best practice, the institution should consider using well-trained IV teams (6,11,12), which is the most effective way to reduce peripheral IV catheter–related infectious complications.(8)

Wrong Turn through Colon: Misplaced PEG

The Case

An 87-year-old man was admitted for congestive heart failure (CHF) exacerbation. In addition, a past cerebrovascular accident (CVA) with resulting dysphagia required placement of a feeding tube. The feeding tube was a percutaneously placed gastric tube, placed by gastroenterology 1 month before admission.

During hospitalization, the patient tolerated his tube feeds until hospital day 4, when he developed loose stools. The diarrhea progressed with liters of watery stool daily, necessitating placement of a rectal tube. Various stool studies were sent and failed to reveal an etiology. Bulking agents were added to his tube feeds but did not improve the consistency or volume of his stools. The primary team noted a remarkable similarity in appearance between the tube feeds and the stool. During a tube check, it was discovered that the tip of the feeding tube was in the colon and not the stomach.

On further investigation, it was determined that a loop of colon was overlying the stomach when the tube was placed. Consequently, while entering the stomach, the gastroenterologists inadvertently passed through the colon. Over time, a fistula formed between the stomach and the adjacent bowel (through which the tube passed during insertion); ultimately, the tube migrated back into the colon, which meant that the feedings were bypassing the entire digestive apparatus of the small intestine.

After the error was recognized, another tube was placed in the stomach and the previously placed tube was removed. However, the delay in identifying the problem resulted in sustained inadequate nutrition and significant decompensation.

Residual Anesthesia: Tepid Burn

The Case

A 42-year-old Filipino man presented to an outpatient surgery center for scheduled repair of an anal fistula. The patient received pre-procedure anesthesia with a "saddle block" and underwent a successful intervention. When his anesthesia block began to wear off, he was deemed safe for discharge and instructed to take sitz baths with tepid water.

One month later, the patient returned for a second evaluation under anesthesia, and the surgeon noted scarring on the patient's buttocks and proximal posterior thighs. There were also large areas of healed burns and associated skin changes. Additional history from the patient and his wife indicated that they misunderstood the term "tepid" and used scalding hot water for the sitz baths. It also appears the patient's slowly resolving saddle anesthesia in the first 24 hours home blunted his response to the hot water. Unfortunately, the patient did not seek additional medical attention. It was felt that challenges with both health literacy and language barriers contributed to the patient's failed understanding of discharge instructions.

No News May Not Be Good News

The Case

A 10-year-old girl with a history of asthma was brought by her mother (a nurse) to see a pediatrician because of a 15-pound weight loss over a period of 3 months. There were no notable changes in the child's diet or urination and there were no other systemic symptoms. A physical examination was unremarkable and the pediatrician ordered basic labs on a Thursday morning.

On Monday morning, the patient's mother called the pediatrician's office to obtain the results of the blood tests. The pediatrician was busy all day long but near the end of the day found the result. He was shocked to learn that the patient's blood sample, drawn on Thursday, had a glucose level of 320 mg/dL (normal random blood sugar: 70–125 mg/dL).

The pediatrician immediately contacted the mother and had her bring her daughter to the office. A repeat stat blood test showed that the patient's blood sugar was now 450 mg/dL and she had moderate ketones on a urinalysis (showing early signs of diabetic ketoacidosis, which can be life threatening). She was given insulin and specific instructions on management at home. The patient and mother had to return to the clinic each day for the next few days for ongoing management. The patient did not experience any long-term consequences.

When reviewing the case, the pediatrician was surprised that no one had been notified about the elevated blood sugar level. He came to learn that a fax of the laboratory results had been sent to the clinic on Saturday with the urgent result, but, for unclear reasons, the physician covering for the weekend never saw the result. This clinic did not have an electronic medical record (EMR).

Sloppy and Paste
The Case

A 78-year-old man with hypertension and diabetes presented to an emergency department (ED) with new onset chest pain. The ED physician reviewed the patient's electronic medical record (EMR) and noted a history of "PE" listed under the Past Medical History section. This raised his suspicion for the possibility of a pulmonary embolus (PE). After initial testing excluded a cardiac etiology, a computed tomography (CT) scan of the chest was ordered to rule out a PE. When the physician approached the patient to explain why he was ordering the diagnostic test, the patient denied ever having a PE or being treated with blood thinners.

Puzzled by the conflicting reports, the ED physician returned to the EMR and noted that this mistaken history of PE dated back several years. It even appeared in the "problem list" section of his EMR. Investigating further back, the ED physician discovered that the letters "PE" were first noted nearly a decade earlier where it was clearly intended to reflect a "physical examination" rather than a "pulmonary embolus." A physician likely copied and mistakenly pasted "PE" under "past medical history," after which this history of pulmonary embolism was carried forward time and time again. The patient, who was ultimately discharged from the ED, never suffered any harm from the documentation error. The EMR was updated to reflect, "This patient never had a pulmonary embolism."

Misleading Complaint

The Case

A 54-year-old homeless man with a history of alcoholism presented to the emergency department (ED) with complaints of knee problems. The triage nurse documented the chief complaint as "bilateral knee pain" and left the chart for the ED physician. The patient had not experienced any trauma to the knees and had no other symptoms; a focused physical examination of the knees was unremarkable. The ED

physician diagnosed the patient with a musculoskeletal injury and prepared to discharge him. After receiving his discharge instructions, the patient tried to get up and walk but was noted to be unsteady. A subsequent full neurologic examination raised additional concerns and a diagnostic head computed tomography (CT) showed a subdural hematoma. The patient was admitted for urgent neurosurgical intervention.

Given the near miss of an unsafe discharge and the initial diagnostic error, the hospital's quality committee formally reviewed the case. The triage nurse reported that the patient used a number of vague and varied complaints about his knees, such as: "giving out," "couldn't walk on them," and "feeling wobbly." The nurse simply summarized the descriptions with the term "bilateral knee pain." The ED physician relied heavily on this documented triage complaint, leading to an overly focused history and examination.

Not-So-Therapeutic Tap
Case & Commentary—Part 1:

A 67-year-old woman with a history of cirrhosis who was status post cholecystectomy was admitted at midnight with worsening ascites and abdominal pain. As part of the evaluation of the abdominal pain (to rule out spontaneous bacterial peritonitis) and to relieve the symptoms of abdominal distention, the admitting team (comprised of a second-year resident and an intern) decided to perform a diagnostic and therapeutic paracentesis (removal of fluid from the abdomen).

The second-year resident had performed 6 paracenteses as an intern so felt reasonably comfortable with the procedure. While she had not taken a formal ultrasound training course, she had been informally taught how to use the ultrasound to identify the fluid to perform the paracentesis safely. The resident felt comfortable proceeding with the procedure with the intern, who had never done one before, so she did not call the night hospitalist, who was available to supervise procedures overnight.

Medical educators champion evidence-based medicine for everything except the methods used to educate. By neglecting advances in our understanding of how medical trainees learn, educators miss a major opportunity to improve graduates' skills and patient safety. Serious or fatal iatrogenic complications occur in 2.9% to 3.7% of hospitalized patients (1), and medical procedures are the second most common cause of these complications.(2,3) Many procedures in teaching hospitals are performed by unsupervised trainees.(4,5) For generations, a pardigm known as "see one, do one, teach one" was used to ensure unsupervised trainees were capable of performing procedures. This form of vicarious learning allowed trainees to perform procedures after watching one, and allowed teaching the procedures to other trainees after performing only one. The traditional "see one, do one, teach one" approach to teaching procedural skills exposes patients to substantial risk of harm from trainees who are not yet fully competent.

Safely performing and teaching procedures in academic hospitals can be challenging. While guaranteed faculty supervision might seem like an answer, it is unclear whether supervision of trainees prevents complications because not all internists and hospitalists who supervise trainees routinely perform procedures themselves.(6,7) In fact, trainees sometimes have more knowledge about the procedure than the supervisor. In the above case, we are not told whether the night hospitalist was adequately trained to safely perform a paracentesis. Therefore, we cannot be confident that requiring the presence of a supervisor prevents complications.

On the other hand, if the trainee was reliably competent, there is no reason to require supervision (aside, perhaps, for billing purposes). One could imagine that competence to perform a procedure safely and effectively is determined by the experience of the clinician (i.e., number of previous procedures

performed). However, experience alone does not guarantee competence.(8) Studies show that the number of procedures performed does not correlate with competence for central venous catheter insertion (9-11), thoracentesis (12), lumbar puncture (13), or paracentesis.(14) If the 6 paracenteses previously performed by the resident in this case had been performed incorrectly, the procedure might continue to be performed incorrectly for the remainder of this physician's career. The resident could then propagate this incorrect performance through teaching interns and medical students.

In contrast, highly trained and skilled personnel who perform many procedures achieve low complication rates.(15,16) This highlights a central point: practitioners and educators must distinguish the major difference between experience and expertise. Experts reach the highest level of achievement for a given task and maintain that level of proficiency through deliberate practice over time.(17) Expertise, instead of experience, is a more useful predictor of high reliability and safe systems.(18) The number of procedures required to attain expertise varies widely and unpredictably. In the past, the American Board of Internal Medicine (ABIM) required residents to perform and document 5 procedures to be considered competent.(19) However, after data emerged showing internists in practice were not performing many procedures (6,7) and after realizing that 5 procedures were not enough to ensure competency, the ABIM dropped their competency requirement.(19) ABIM no longer requires competency for many bedside procedures.(19) Despite the lack of evidence of a threshold volume–competency linkage, many hospitals still use 5 procedures as the cutoff for clinicians to obtain privileges to perform internal medicine procedures. Self-assessment of skill or confidence does not correlate with the ability to perform a competent procedure (10,12-14,20) and should never be used to determine a clinician's capabililty.

Multiple studies show that traditional medical education methods do not yield competent trainees. A study of 40 graduating internal medicine residents showed that not one could adequately perform a simulated thoracentesis procedure (removal of fluid from the pleural space).(12) The residents' average test score on a skills checklist was 52% items correct.(12) This study was performed at the time when ABIM still expected graduating internal medicine residents to be competent in thoracentesis (requirements were subsequently changed). Failure of the "see one, do one, teach one" approach to procedure training was also confirmed in evaluations of graduating nephrology fellows' ability to insert a temporary dialysis catheter (11) and neurology residents' ability to perform a lumbar puncture (13)—both procedures are required for certification at graduation in respective training programs. It is clear that the old model of procedure training has been ineffective, places patients at risk for injury, and is inadequately preparing trainees for future practice and teaching.

Case & Commentary—Part 2:

With the ultrasound, the resident and intern found what appeared to be a safe place to obtain the ascites fluid, 8 cm below her cholecystectomy scar, and proceeded with the tap. After collecting about 700 cc of clear yellow fluid, the ascitic fluid became blood-tinged, and the catheter was removed. At the time, the patient did not complain of abdominal pain—she actually felt improved—and her vital signs were stable.

About 20 minutes later, the intern was called due to the patient's complaints of lightheadedness with a blood pressure of 70/40 mm Hg (down from 110/65 mm Hg). The patient appeared pale and was complaining of increased abdominal pain. Her abdomen was tense and tender. With concerns for acute bleeding into the peritoneum, the resident and intern began resuscitation and contacted the night hospitalist. Interventional radiology and general surgery were quickly consulted.

A stat angiogram revealed a bleeding omental vessel that was pressed against the abdominal wall because of an adhesion, likely secondary to the patient's previous cholecystectomy. The interventional radiologist was unable to embolize the vessel, so the patient underwent emergent laparotomy with

removal of liters of clotted blood and ligation of the affected vessel. She had a prolonged course in the intensive care unit (ICU) but ultimately survived and was discharged to a rehabilitation facility 3 weeks later.

It is unclear whether further training or supervision could have prevented the complication in this case. Even highly competent operators occasionally injure patients. However, use of rigorous evidence-based methods for procedure training, such as simulation-based deliberate practice (17) and mastery learning (21) decrease the overall rate of procedure complications.(9,22) As an educational framework, mastery learning allows medical educators to ensure competency before trainees are allowed to work with actual patients. Mastery learning requires that all learners meet or exceed a minimum passing score on a skills test before the completion of training. This means that training time varies while education outcomes are constant.(21) In other words, a struggling trainee may require 10 hours to reach the same level of competency that another trainee achieves in 4 hours.

One recognized way to achieve mastery is through the use of simulation.(23) Extensive research documents that simulation-based procedure training increases the knowledge and skills of trainees while assuring competence (9-14,24) and improving health care quality and patient safety.(9,10,22,25-28) Evidence shows that using simulation to teach procedures, such as colonoscopy (25), laparoscopic cholecystectomy (26), advanced cardiac life support (27), and bronchoscopy (28), can improve patient outcomes.

Most published studies in simulation feature standardized training time and content without requiring a minimum standard of proficiency (mastery learning). Our research group documented how medical simulation training using the mastery learning model improves clinical skills for bedside procedures such as paracentesis (14), lumbar puncture (13), thoracentesis (12), and central venous catheter insertion.(9) Additionally, the risk of procedure-associated injury is significantly reduced using this technique for central venous catheter insertion.(9,22) Simulation-based mastery learning (SBML) for central venous catheter insertion improves skills (9-11), retention of skills (29), patient care (9-10), and outcomes (22), while reducing hospital costs.(30) In a recent systematic review, mastery learning was featured in a subset analysis as showing a potential benefit in learning outcomes.(31)

Seldom used in medical education in the United States, SBML's innovative approach may transform how educators train physicians. Traditional models of medical education use bell-shaped curves and 2 standard deviation criteria for passing. This results in many trainees passing examinations despite unacceptably low performance. For medical procedures and other clinical competencies, this is not acceptable because of the high stakes of patient complications and medical errors. SBML requires trainees to reach a high level of achievement on a simulator before being allowed to work directly with patients. Thus, learners truly become experts. The SBML minimum passing score is set at a high level by experts in the field that understand the implications of errors on patients. Moreover, the use of SBML reduces skill variation among trainees so poor performers are not applying their inadequate clinical skills to patients—the major problem with traditional training methods. Studies show small standard deviations (variation) in the posttest skill performance of trainees who have undergone SBML for lumbar puncture (13), paracentesis (14), central venous catheter insertion (9), and advanced cardiac life support.(24)

Some argue that medical resources should not be used to train internal medicine residents on bedside procedures because internists and hospitalists are no longer performing procedures. With internists' and hospitalists' busy schedules and the availability of Interventional Radiology (IR) physicians who perform a large volume of procedures (2,6,7), many clinicians feel that it is best for procedures to be performed in IR. Despite this reasoning, trainees are still performing the majority of procedures in academic hospitals. Although one may argue that patient care is better when experts perform procedures, there is no evidence

that care is better when procedures are performed in IR instead of at the bedside by trained internists. In fact, patients are highly satisfied with bedside procedures performed by hospitalists and trainees (32), these procedures can be done safely (with proper training), and delays in scheduling an IR procedure can potentially increase hospital days and overall patient costs (unpublished data; submitted). In some instances it may be dangerous for a sick patient to leave the bedside to go to IR for a procedure.

In conclusion, medical educators need to ensure that future clinicians are properly trained and evaluated so that they can perform bedside procedures such as paracentesis. Direct supervision, the number of procedures performed, and self-assessment of confidence or competency do not predict the safety of bedside procedures. Therefore, SBML should be used to achieve this aim because it improves procedures skills, ensures trainee competency, reduces skill variation among trainees, and improves clinical outcomes with lower costs.

Comanagement: Who's in Charge?

The Case

A 77-year-old man with a history of chronic obstructive pulmonary disease (COPD) was admitted with a left hip fracture to the orthopedic surgery service, which has internal medicine hospitalists comanage its patients. The surgical repair went smoothly. On postoperative day 2, the patient was doing well when seen by the comanaging hospitalist. Later that day, the patient's oxygen requirement increased and the patient noted that he was feeling somewhat more short of breath compared to his baseline. The nurse notified the orthopedic surgery resident of the change in clinical status. A chest x-ray, ordered by orthopedics, showed new bilateral basilar consolidations. The orthopedic resident did not communicate these findings to the hospitalist, nor did he start antibiotics. The orthopedic resident assumed that the hospitalist was keeping up-to-date on developments and would initiate the appropriate treatment, while the hospitalist assumed that he would be contacted with any change in clinical status.

When the hospitalist next saw the patient (postoperative day 3), the patient was even more hypoxic. A computed tomography (CT) angiogram was done, which was negative for pulmonary embolism but showed much more extensive consolidations of his bilateral lung fields. He was started on broad-spectrum antibiotics; however, the patient's respiratory status continued to decline. He was ultimately transferred to the intensive care unit (ICU), intubated, and later died of hypoxic respiratory failure and sepsis (presumably from his pneumonia). It was believed that the delay in diagnosis of pneumonia and initiation of antibiotics may have contributed to the patient's downhill course.

A Painful Dilemma

The Case

A 47-year-old woman with end-stage renal disease due to polycystic kidney disease was admitted with fever. She was taking propoxyphene or hydrocodone at home for pain. She has had multiple admissions associated with electrolyte abnormalities due to nonadherence with her outpatient dialysis schedule. Because her permanent arteriovenous (AV) graft normally used for dialysis was clotted and unusable, the patient had been receiving dialysis via a temporary catheter placed in her left femoral vein.

Given that her new presentation included fever, blood cultures were drawn, ultimately growing yeast. An echocardiogram revealed a large tricuspid valve vegetation. The patient's temporary dialysis catheter in her left femoral vein was removed and a new one placed in the right femoral vein. The unused clotted AV graft in the left arm remained in place, and the patient was transferred to a tertiary hospital for consideration of surgery for fungal endocarditis.

The case management department reviewed this case. Their assessment was that the patient's nonadherence to dialysis led to clotting of her permanent AV graft, which necessitated use of temporary femoral vein access. Femoral intravenous catheters are associated with significantly increased risk of infection, including fungal infection, when compared with the use of permanent AV grafts. Moreover, the case management department felt that her nonadherence to dialysis was encouraged by the primary physician's prescription of opiates.

Although this patient was believed to be addicted to narcotics, she was never formally diagnosed with an addiction. Her providers suspected that she often intentionally skipped dialysis sessions, became uremic or volume overloaded, then presented to the emergency department for treatment and admission to the hospital. After admission, her primary physician would usually order intravenous (IV) hydromorphone (Dilaudid) to be given for "body pain." The patient would ask the nurses to "push the hydromorphone fast" and flush after the medication (saying that the previous nurse would push it fast) and ask for dose escalation. When a substance abuse evaluation was recommended to the patient, she repeatedly declined it.

Transfer Troubles

The Case

An orthopedic surgeon at a small community hospital contacted an emergency department (ED) physician at a large academic medical center about a patient transfer. At this hospital, standard procedure called for all transfers from outside hospitals to be seen and evaluated in the ED. The orthopedic surgeon briefly described a 92-year-old woman with a history of dementia who had a left hip fracture. They had taken her to the operating room, but she developed low blood pressure before the case and the anesthesiologists were not comfortable managing her care at the community hospital. The referring orthopedic surgeon also spoke with the on-call orthopedic surgery resident at the tertiary care center and conveyed the same brief history. Minimal other clinical details were discussed.

The patient was transferred to the tertiary care center and was clinically stable on arrival to the ED. None of the notes or clinical documentation from the referring hospital arrived with the patient other than her demographic data. She was quickly admitted by the orthopedic surgery resident and prepped for surgery the following morning.

Early the next day, the patient was taken to the operating room for surgical repair of her hip fracture. During induction of anesthesia, the patient rapidly became hypotensive and required vasopressors. The surgical team proceeded, but the case was complicated by significant hemodynamic instability. The patient survived the surgery, but experienced persistent postoperative hypotension (shock) of unclear cause and could not be weaned from the ventilator. Ultimately, care was withdrawn and she died a few days after surgery.

Notably, following her operation on hospital day 2, medical records arrived from the referring hospital and the anesthesia notes were reviewed. They were handwritten and difficult to read but described "profound hypotension" at the start of the case and that the patient had actually suffered a full cardiac arrest (written as "unable to obtain BP...no palpable pulse...arterial access...case cancelled, to PACU."). There were few other details in any of the notes about the cardiac arrest.

Although it was not completely clear to the orthopedic team or anesthesiologists what happened, all agreed that her case would have been managed much differently had they known more about the events at the referring hospital and that such knowledge could have potentially prevented her death.

The Forgotten Line

The Case

An 81-year-old man with a history of coronary artery disease, hypertension, cerebrovascular accidents, and chronic kidney disease was transferred to a referral hospital for percutaneous coronary intervention after presenting to a community hospital with hypotension and chest pain. At the community hospital, a central venous catheter was placed in the patient's right internal jugular vein for administration of vasopressors. When he arrived at the referral hospital, he was hemodynamically stable and the vasopressors had been discontinued for an unspecified period of time, although the central line remained in place "just in case." The patient underwent successful stenting of his coronary arteries and was discharged to an assisted living facility within 48 hours of admission.

On arrival at the assisted living facility, it was discovered that the central line was still in place. The caregivers at the assisted living facility noticed the line and returned the patient to the referral hospital the same day to have the central line safely removed. The incident was reported and investigated, revealing several contributing factors. First, the patient was a transfer who was admitted late at night, and who was signed out the next morning as 1 of 12 holdovers to the admitting teams. Second, it was "switch day" for the interns and early in the academic year, so many of them were still getting used to a new system. Third, the line had been placed somewhere else, for an indication (hypotension) that no longer existed, and it had not been used at any point during his 48-hour admission. Lastly, while the nurse noticed the line during the routine predischarge examination, she assumed that the patient was supposed to be discharged with it in place and did not call anyone from the medical team to get clarification.

Double Dose at Transfer

The Case

A 74-year-old man with history of diabetes and hypertension was admitted to the emergency department (ED) for left lower extremity pain, swelling, and erythema. The ED physician made the diagnosis of cellulitis and prescribed vancomycin, 1 g IV every 12 hours. The patient's first dose was administered in the ED.

Approximately 6 hours after admission to the ED (and just 3 hours after receipt of his first vancomycin dose), the patient was transferred to a medical–surgical floor. The admitting nurse noted the vancomycin order on the admission order set and—unaware that the patient had received a dose in the ED—administered another dose.

Physicians may write "delayed admission orders" that are activated upon ward admission. However, in patients with longer ED stays, some of those delayed admission orders are carried out in the ED. In this instance, the respective ED and ward systems were not linked, limiting tracking of medication administration in the respective units. Similarly, the pharmacy system at this hospital did not capture outpatient versus ED versus ward dispensing of medications.

A physician who was aware the patient had received a dose of vancomycin in the ED realized the mistake and ordered a serum vancomycin level. While the patient was confirmed to have an elevated level, he experienced no associated toxicities, and his dosing resumed on the appropriate schedule.

The Perils of Cross Coverage

The Case

A 70-year-old woman was admitted to the intensive care unit (ICU) with acute change in mental status a few days after lumbar laminectomy. Her medical history was significant for a ventriculoperitoneal (VP) shunt for suspected normal pressure hydrocephalus. She was febrile with nuchal rigidity. Her white blood cell (WBC) count was over 20,000 cells/μl. Blood cultures were positive for *E. coli*, and appropriate antibiotic therapy was initiated. The patient responded well—she began to have brief but meaningful conversation with her family. Her WBC started to trend down, and she was afebrile for 48 hours.

On day 4 of her ICU admission, a Friday, she exhibited fluctuating mental status with prolonged episodes of drowsiness. The ICU team attributed this to recent use of sedatives. Signout to the incoming night float team did not highlight the change in mental status. Over the course of the ensuing night she became drowsier. The night float team assumed it was her baseline mental status. After transfer to the incoming cross-covering team for the weekend, the patient was found comatose.

Magnetic resonance imaging (MRI) showed ventriculitis with possible infectious cerebritis. The patient developed generalized tonic clonic seizures and was treated with IV phenytoin. She was emergently transferred to surgery for removal of the VP shunt and placement of ventricular drain for intraventricular gentamycin. The patient received 8 days of intraventricular gentamycin with resolution of ventriculitis as documented by negative *E. coli* cultures from the ventricular cerebrospinal fluid. She made a gradual recovery after spending 6 weeks in the ICU.

Subsequent root cause analysis determined that earlier recognition of the change in mental status might have altered the patient's course. It identified inadequate signout to the night float team as the primary reason why that team did not identify the patient's deteriorating mental status.

Turn the Other Cheek

The Case

A 56-year-old man underwent two skin biopsies to evaluate clinically concerning lesions. The first biopsy was diagnostic for squamous cell carcinoma (SCC) and documented as "left cheek" in the health record. The second biopsy was consistent with an atrophic solar keratosis (a benign finding) and the site was documented as "left inferior orbit."

The patient was then referred to a dermatologic surgeon to have his SCC excised. The accompanying referral documentation included a diagram of a face with the SCC biopsy site marked by an "X" on the left cheek. The pathology report included a description of the anatomic location that was also noted as "left cheek." On the day of surgery, standard preprocedure verification was completed. The surgery site was marked after the patient confirmed the biopsy site with use of a mirror, two physicians identified a biopsy scar within a clinical lesion on the left cheek, the diagram from the referring physician was reviewed, and the anatomic description of the site from the pathology report was confirmed. The surgeon then excised a lesion on the left cheek.

The patient returned to his referring physician, who immediately realized that the wrong lesion (the benign solar keratosis) had been excised. The patient returned to the surgeon to report the mistake. On closer review, he realized that the actual site of the SCC was, while nominally on the left cheek, more specifically near the preauricular skin. The lesion excised was the one referred to as "left inferior orbit" rather than "left cheek"—an error that resulted from ambiguity in the description and the patient's self-

identification of the wrong lesion. The patient required a second surgical excision to remove the SCC lesion.

Cultural Dimensions of Depression

The Case

A 55-year-old Vietnamese man was admitted to a general medicine ward with vague complaints of inability to breathe and swallow. The patient had been living in the United States for 20 years and currently was unemployed, with a wife and two children. He spoke English reasonably well; nevertheless, the history was obtained with a translation service. The patient was anxious and repeatedly stated that he was "dying" from his physical ailments. Extensive workup showed no evidence of cancer, but revealed reflux disease and Zenker diverticulum (an outpouching) of the esophagus. Psychiatric evaluation ruled out major depression. In the midst of a gastroenterology consult (to obtain an esophagogastroduodenoscopy [EGD]) the patient ran to the bathroom, jumped out of the fifth floor window, and killed himself.

After this event, subsequent discussions with the family revealed some relevant details. The patient had lived through the Vietnam War; he and his family had come to the United States on a boat as part of a mass exodus in the late 1970s; there was strife within the family unit, as the patient felt he was an undue burden to them; and the family was "losing face" in their community due to his unemployment.

The psychiatric team concluded that the evaluation had not been sufficiently sensitive to identify important culture-specific clues related to depression and has since taken steps to incorporate culturally sensitive screening tools.