Changing the Culture Around Cultures

A 5-day-old female infant presented to a children's hospital emergency department (ED) with jaundice. She was born at 38 weeks', 4 days' gestation with a weight of 3400 g after an unremarkable pregnancy and perinatal course. By parental report, a 36-hour bilirubin level was 9 mg/dL, and she did not receive phototherapy. Her mother's blood type was B, Rh positive. The baby was exclusively breastfed, nursing every 2 to 4 hours for 20 minutes per breast. Voiding and stooling patterns were appropriate. In the ED, she was afebrile and well appearing with a weight of 3380 g. At 130 hours after birth, her total serum bilirubin (TSB) was 19.4 mg/dL. The ED provider decided to admit the patient for intensive phototherapy. During her observation in the ED, the infant had acute decreases in oxyhemoglobin saturation by pulse oximetry (SpO_2) to 90% while asleep, self-resolving within seconds. Therefore, the ED provider initiated a partial sepsis evaluation including blood culture, complete blood count with differential, and C-reactive protein. The complete blood count and C-reactive protein were normal. While an inpatient, she received phototherapy for 6 hours and was discharged from the hospital after an appropriate postphototherapy TSB.

At 27 hours of incubation on continuous monitoring, Gram-positive cocci in clusters were detected from the blood culture. The discharging inpatient team referred her back to the ED for further evaluation. The patient had remained afebrile without changes in her activity, breastfeeding, or urine output. An interval weight was appropriate. In the ED, sepsis was presumed given "young age and early growth [of the blood culture]." Therefore, a full evaluation for neonatal sepsis including lumbar puncture was performed. The evaluation was completely reassuring without signs suggestive of infection. She received empirical ampicillin and cefotaxime. Just before inpatient admission, the Verigene BC-GP assay (Nanosphere Inc, Northbrook, IL) identified *Staphylococcus epidermidis*. The ED provider considered it pathogenic, so vancomycin was also given. After arrival to the inpatient unit, the admitting hospitalist consulted with the infectious diseases department, and it was agreed that the blood culture was a contaminant. In the setting of a reassuring clinical course and examination, the patient was discharged to home with close outpatient follow-up.

As health care professionals, we strive to deliver high-value care, which can be considered aiming for the highest quality outcomes at lowest possible costs. This case illustrates how 1 test begets more interventions, which beget even more interventions. How did the common scenario of neonatal hyperbilirubinemia culminate in 2 inpatient admissions, a full sepsis evaluation, and administration of broad-spectrum antibiotics? Four pivotal decisions propelled the cascade of

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value, quality, cost, hyperbilirubinemia, blood culture, contaminant

ABBREVIATIONS
AAP: American Academy of Pediatrics
CoNS: coagulase negative *Staphylococcus*
ED: emergency department
SpO_2: oxyhemoglobin saturation by pulse oximetry
TSB: total serum bilirubin
TTD: time to detection

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interventions. The following discussion examines each of these and explores the value, effectiveness, and efficiency of the medical care delivered.

The first decision is whether to start phototherapy. According to the American Academy of Pediatrics (AAP) Guidelines for Management of Hyperbilirubinemia, this infant's TSB was below the phototherapy threshold of 21 mg/dL.[1] Inpatient phototherapy was not necessary. Newman et al estimated the number needed to treat with inpatient phototherapy to prevent 1 infant from developing a TSB at which the AAP recommends exchange transfusion.[2] For 38- and 39-weeks' gestational age female infants meeting the phototherapy threshold at 72 hours of life or greater, the numbers needed to treat are 705 and 1516, respectively. In the setting of physiologic hyperbilirubinemia not meeting the phototherapy threshold, the highest value decision may have been discharge to home with next-day outpatient follow-up, if available. That decision would advance quality by maintaining safe and effective care while minimizing financial costs and psychosocial stress to the family.

The second decision is initiating the partial sepsis workup, driven by a concern for pathologic hypoxia in the setting of hyperbilirubinemia. One must ask, what is the probability of sepsis in this infant? As we have already established, the TSB was below the AAP phototherapy threshold and therefore not truly pathologic. Regarding the oxyhemoglobin desaturations, infants may have clinically unapparent, intermittent hypoxic episodes while asleep. Data from the Collaborative Home Infant Monitoring Evaluation (CHIME) Study Group have shown that 60% of healthy, term infants have at least 1 desaturation episode (defined as SpO_2 <90% lasting at least 5 seconds) during a 3-minute epoch of monitor use.[3,4] The highest incidence of desaturations occurred in infants at younger ages and "appear to be part of normal breathing and oxygenation behavior." With this definition, the episodes in our reported patient are within the range of normal behavior. In the absence of fever, hypothermia, lethargy, irritability, poor feeding, respiratory distress, or apnea, these transient dips in SpO_2 provide little extra information. In summary, neither the brief hypoxic events nor the hyperbilirubinemia represent sepsis risk factors.

Does the blood culture serve as a safety net, "just in case?" A recent study by Parikh et al titled "Do We Need This Blood Culture?" investigated blood culture utilization in low-risk patients with common pediatric inpatient diagnoses of community-acquired pneumonia, asthma, bronchiolitis and skin and soft tissue infections.[5] They found high rates of negative or contaminated blood cultures, low rates of clinically significant positive blood cultures, and overutilization of blood cultures. There were high rates of a low-value test. None of the children benefitted from their blood culture, and some experienced harm such as adverse effects of antibiotics, unnecessary hospitalization, additional testing, and familial stress. Estimates of blood culture contamination rates are generally 2% to 5% but may be up to 12%, varying by several factors including institution, volume of blood, antiseptic method and role of the collector (eg phlebotomist or resident).[6–10] The likelihood of contamination may actually be greater than the likelihood of bacteremia.

The concern for sepsis was heightened when the blood culture returned positive at 27 hours. This led to a full sepsis workup, broad-spectrum antibiotics, and inpatient readmission, representing the third set of interventions in the cascade. How does one interpret a positive blood culture at 27 hours in this neonate without risk factors? Evans and Fine evaluated blood, urine, and cerebrospinal fluid culture time to detection (TTD) in infants 0 to 90 days old within ED and inpatient settings.[11] Fever was not an inclusion criteria, and determinations of true positives versus contaminants were classified based on the attending physicians' decision to treat. Of all blood cultures, true pathogens had a mean TTD of 13 hours, whereas contaminants had a mean TTD of 25 hours. The mean TTD for all blood cultures positive for coagulase-negative *Staphylococcus* (CoNS) was 28 hours. This study alone does not provide sufficient assurance that growth of Gram-positive cocci at 27 hours in a neonate is a contaminant. However, the paucity of sepsis risk factors and the patient's reassuring clinical course certainly decrease the likelihood of true infection. In retrospect, perhaps collaboration between the referring inpatient team and the ED team would have optimized diagnostic and management decisions in the face of uncertainty.

The addition of vancomycin to treat CoNS represents a fourth level of intervention in the flow of clinical care. How does the identification of CoNS, a common contaminant, influence the probability of true bacteremia? Factors associated with pathogenic CoNS infection include admission to an ICU, presence of an intravascular catheter, clinical findings of infection,

growth in ≥2 blood cultures, growth from 1 blood culture and 1 sterile site (eg, cerebrospinal fluid), or growth within 15 hours on a continually monitored blood culture system.[12] The lack of specific risk factors for CoNS further decreases the likelihood of true bacteremia.

We recognize the overwhelming desire to deliver safe and effective care in the setting of uncertainty. The stakes are high in the neonatal population, and the consequences of serious bacterial infection in the neonate should not be overlooked. However, delivering more care does not necessarily mean delivering higher value care. Available information at each decision point lowered the probability of neonatal sepsis, yet the intervention cascade continued. The baby did well but, looking back, one should ask if it was due to or despite medical interventions. The resource overutilization did not necessarily increase the value of the experience.

As Schroeder et al ask, how can we safely do less?[13] How can we maintain high-quality, effective, patient-centered medical care and simultaneously minimize utilization, costs, and inefficiency? As health care professionals, we have an ongoing duty to turn data into useful information that guides our decision-making in the face of uncertainty. Ultimately, decision support systems should improve our ability to routinely incorporate pretest probabilities with accruing history, examination, and diagnostic test results on subsequent posttest probabilities. Until then, we ought to pause as the flow of clinical care proceeds and ask if we are truly maximizing the chance of good outcomes while minimizing risks with each decision we make.

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