Value of Superficial Cultures

Diagnosing neonatal sepsis in a community hospital

BOSCO A. PAES, MD, FRCPC
ANJANA MODI, MD, FRCPC

SUMMARY

In a study of babies younger than 2 weeks who were admitted to a community neonatal facility with suspected sepsis, pathogenic organisms grown from superficial swab samples were compared with those from deep cultures to meet the gold standard definition of true sepsis. We conclude that superficial cultures have limited value in the diagnosis of neonatal sepsis in a community setting.

RÉSUMÉ

Dans une étude des nouveau-nés de moins de deux semaines admis dans une unité néonatale communautaire à cause d'infection superficielle ou suspecte, on a comparé les organismes pathogènes cultivés à partir de prélèvements superficiels aux pathogènes provenant de cultures profondes pour satisfaire la définition classique de la septicémie véritable. Nous concluons que les cultures superficielles ont une valeur limitée pour le diagnostic de la septicémie néonatale dans un contexte communautaire.

SYSTEMIC BACTERIAL INFECtions occur during the first few weeks of life in 1 to 10 babies per 1000 live births. Bacterial sepsis in the newborn is markedly influenced by a host of factors, including prematurity, predisposing maternal conditions, and the use of intensive life-support techniques postnatally.[1] Despite current advances in antimicrobial therapy, bacterial infections continue to be one of the most significant causes of neonatal morbidity and mortality.

Physicians involved in caring for newborns have no single test that can be confidently relied upon to predict neonatal sepsis. The diagnostic approach focuses on a history and review of non-specific signs and symptoms,[2] a complete physical examination followed by screening tests,[3,4] and cultures from superficial and deep body surface sites. In the initial laboratory evaluation of neonatal sepsis, blood, urine, and cerebrospinal fluid are the most commonly cultured deep sources, while superficial cultures include an evaluation of the gastric aspirate and several swabs from the ear, nasopharynx, umbilicus, skin, and rectum.

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Dr Paes is Director of Nurseries at St Joseph's Hospital and is Associate Professor in the Department of Pediatrics (Neonatal Division) at the Children's Hospital of Chedoke-McMaster Hospitals, Hamilton, Ont.
Dr Modi is a Pediatrician in the Department of Pediatrics at St Joseph's Hospital.

Practices are dictated by the concept that superficial colonization of an infant by potential pathogens precedes deep colonization of the body. Presumably, the early identification of these pathogens will guide therapy and avoid serious sequelae.

METHOD

Study setting

St Joseph's Hospital in Hamilton, Ont, is a level II perinatal care facility with an average of 2800 deliveries per year and is part of a comprehensive regional health care program.[5] The hospital's mandate under the three-level system of perinatal care is to diagnose and treat low- to moderately high-risk pregnancies and neonatal problems. The neonatal unit is a 22-bed facility with an average of 1450 admissions yearly. The neonatal unit maintains an effective liaison with McMaster University Medical Centre, referring extremely high-risk patients to the tertiary care unit for ongoing management.

Patients

During the 6-month study period, researchers reviewed the charts of 205 consecutive infants admitted with a diagnosis of suspected sepsis who had body fluid cultures evaluated. The assembled study cohort was younger than 2 weeks. The total number of admissions to the unit during the study period was 748, and the total number

Table 1. RESULTS OF CULTURES FROM INFANTS DURING THE 6-MONTH STUDY PERIOD

SITE	NO. (%) OF CULTURES	NO. (%) OF CULTURES WITH PATHOGENS
SURFACE CULTURES	375 (50.5)	86 (22.9)
Nasopharynx and mouth	23 (6.1)	5 (21.7)
Ear	172 (45.8)	28 (16.3)
Gastric	180 (48.0)	53 (29.4)
Umbilical cord	0	0
Skin	0	0
Rectum	0	0
BODY FLUID	367 (49.5)	19 (5.2)
Blood	205 (55.9)	3 (1.5)
Cerebrospinal fluid	22 (6)	0
Urine	140 (38.1)	16 (11.4)
Joint	0	0
Pleural	0	0
Umbilical catheter	0	0
TOTAL	**742 (100)**	**105 (14.2)**

of live births at the hospital over the same period was 1372. All infants studied had both superficial and deep cultures performed on the same day as part of a sepsis screen. Superficial cultures were obtained from either the umbilical cord, ear, nasopharynx, skin, or gastric aspirate, or a combination thereof.

Cultures

All swabs were immediately inoculated into semisolid charcoal transport media (except gastric aspirates, which were collected in sterile containers). On arrival in the laboratory, swabs were subcultured onto blood agar, salt (7.5%)-mannitol (1%) with phenol red, and McConkey media and were incubated overnight at 37°C. Gastric aspirates were inoculated onto blood and chocolate agar and McConkey media. Salt-mannitol medium was specifically used to enhance the growth of *Staphylococcus aureus*, and McConkey media to identify lactose-fermenting and non-lactose-fermenting organisms.

Similarly, deep cultures involved specimens from every infant of either blood, urine, or CSF fluid, and standard microbiological methods were used for the collection, transportation, culturing, and identification of organisms. All blood cultures in the study were obtained from a peripheral vein under aseptic conditions.

Bag specimens were used for urine cultures and were considered positive only if a single organism with more than 100 000 colonies/mL of urine was isolated with accompanying leukocytes in the urine on two consecutive samples. Because our technique of collecting urine samples is not the gold standard (suprapubic needle aspiration of bladder urine),[6] data were analyzed twice; first, counting positive urine cultures as a positive deep culture and again, discounting positive urine cultures. The

isolation of a pathogen from a deep culture site was used as the gold standard to confirm the clinical impression of a systemic bacterial disease.

All superficial cultures obtained during the study on each patient were simultaneously compared with the deep cultures. The relationship and the analysis performed between superficial cultures and deep cultures was identical to the study of Evans et al.[7] A culture was considered true-positive when both the deep and superficial cultures grew the same microorganism. When both deep and superficial cultures were sterile, the superficial culture was classified as true-negative. If the superficial culture grew a pathogenic organism while the deep culture was sterile, or when the deep and superficial cultures revealed a different organism, the superficial culture was called false-positive. If a pathogen was isolated from a deep culture but the superficial culture contained no organism, the superficial culture was labelled false-negative. Superficial cultures, especially gastric aspirates performed immediately following delivery, usually reflect colonization of the vaginal tract and contain multiple pathogens. Any superficial or deep culture containing more than a pure growth of one organism was classed as being a negative culture based on the probability of cross-contamination.

Data analysis focused on the outcome measure that isolates from both the superficial and deep cultures were of the same bacterial species. Based on these criteria, values of sensitivity, specificity, and positive and negative predictive values were calculated.[8]

RESULTS

An inception cohort of 205 consecutive infants with a presumed diagnosis of generalized bacterial infection during the neonatal period was assembled through a chart review. These infants also satisfied the criteria that in every case at least one deep culture was performed in conjunction with superficial cultures on the same day so that the gold standard evaluation of a true-positive pathogen was met. During the study period 748 infants were admitted to St Joseph's Hospital Neonatal Unit. Of these infants,

205 had presumed sepsis, giving a 27.4% incidence of suspected neonatal sepsis. The mean birth weight of the study infants was 2350 ± 420g (standard deviation), and the average length of stay was 4.5 days. Fourteen babies did not meet entry criteria because only blood cultures were done; none of these cultures were positive.

A total of 742 cultures were obtained from the 205 babies: 375 (50.5%) superficial and 367 (49.5%) deep. External ear canal and stomach (gastric aspirate) cultures accounted for 93.7% of the superficial cultures; blood and CSF accounted for 61.9% of the deep cultures.

Of all cultures, 14.1% produced pathogens (*Table 1*), which included Group B streptococcus, *Escherichia coli, Klebsiella, Staphylococcus aureus,* coagulase-negative *Staphylococcus* strains (CONS), enterococcus, and *Pseudomonas.* The yield of pathogenic organisms was higher from superficial cultures (22.9%) than from deep cultures (5.2%). In the overall analysis, 205 infants produced 742 culture comparisons, all of which were used for evaluating sepsis. The overall distribution of matched pathogens was true-positive 1.6%, true-negative 73%, false-negative 3.5%, and false-positive 21.8%. The sensitivity, specificity, and positive predictive values are shown in *Table 2.*

Organisms isolated from the three positive blood cultures included Group B streptococcus, CONS, and enterococcus, while the corresponding superficial cultures were negative. Only six of the 16 infants with positive urine cultures (three with *E coli,* one with Group B streptococcus, and two with CONS) had similar pathogens in a superficial source. The frequency of true-positive results (1.6%) and the positive predictive value of superficial cultures (7%) was low when obtained on the same day as a deep culture.

Clinical purists may suggest that urine cultures are unacceptable as a positive deep culture if not obtained under sterile technique by suprapubic aspiration. Thus the data in *Table 2* were reevaluated to exclude urine cultures. Repeat analyses showed a sensitivity of 0%, specificity of 78%, positive predictive value of 0%, and negative predictive value of 98% with a 1% prevalence of sepsis.

Using the standard Ontario Schedule of Benefits[9] for diagnostic and therapeutic procedures performed by laboratory services based on the relative weighting of labor, material, and supervision for each test, the total expenditure incurred for cultures on 205 infants over the 6-month study amounted to $11 951.59. Superficial cultures accounted for 38% of the total budget. These costs do not take into account costs for nursing time in the preparation and collection of specimens, equipment costs to the hospital, physician billings for procedures, and personnel involved in transporting cultures to the laboratory.

DISCUSSION

Despite the fact that 79% of all neonatal intensive care units in the United States[7] culture superficial sites of newborn infants, the usefulness of such cultures for diagnosing bacterial infection has never been established through prospective, controlled trials. In a recent study,[7] a mixed cohort of infants admitted to the neonatal intensive care unit both from outside and from within the institution were reviewed for a suspected diagnosis of sepsis. The study concluded that surface cultures were of limited value in predicting sepsis in neonates. The Vanderbilt Hospital, however, is a tertiary care referral center with facilities and services for mothers and newborns designated as high risk.[7] Therefore, patient samples could be different from those found in the general population, incurring the problems of both referral filter and centripetal biases.[10] Moreover, the inception cohort was not standardized in the evaluation of sepsis, as infants born outside the institution had routine superficial cultures done, while those born in the hospital were cultured only if sepsis was suspected.

The accuracy of a test depends on its ability both to diagnose infection when it is present (sensitivity) and to diagnose no infection when it is not present (specificity).[11,12] Tests are chosen based on the probability that the patient has the clinical condition for which a test is useful and the test's accuracy in diagnosing the specified disease. A false-positive result will label a healthy person sick, while a false-negative result will lead astray health professionals

not versed in critical appraisal of scientific evidence.[13,14]

The diagnosis of neonatal sepsis currently relies heavily on the physician's clinical judgment and diagnostic acumen. Recognizing that neonatal morbidity and mortality increase rapidly with delay in diagnosis, a number of diagnostic tests have been implemented and evaluated by relating them to proven sepsis.[3,4]

The practice of using superficial cultures to predict pathogenic organisms causing invasive disease continues to be widely accepted despite conflicting evidence in the

Table 2. ANALYSIS OF RESULTS

	BODY FLUID CULTURE		
	+	−	
SURFACE CULTURES +	6 (TP)	80 (FP)	86
SURFACE CULTURES −	13 (FN)	268 (TN)	281
TOTAL	19	348	367

Sensitivity = 31%, specificity = 77%, positive predictive value = 7%, negative predictive value = 95%, prevalence = 5%
T − true, P − positive, F − false, N − negative

literature.[15-19] The Oxford database of controlled perinatal trials and a MEDLINE review clearly indicated that only one study[7] appraising superficial cultures as a diagnostic test met methodological standards.[11] Because the Vanderbilt data cannot be generalized and the inception cohort was not standardized, scientific application to a community-based setting is limited.

In this paper only infants suspected of having a generalized bacterial infection were studied. The sensitivity, specificity, and positive and negative predictive values of superficial cultures were 31%, 77%, 7%, and 95%, respectively. The predictive values were a function of the low frequency of bacterial sepsis, at 5%. Unlike sensitivity and specificity, positive and negative predictive accuracies depend on prevalence.[9,11] It is not surprising, therefore, that with a

prevalence of sepsis ranging between 1% and 5% (depending on how urine culture results are interpreted), the positive predictive value of superficial cultures ranged between 0 and 7%. In this regard, the low prevalence of sepsis and the high cost of surface cultures does not make the practice cost effective.[20] Moreover, superficial cultures can lead to inappropriate use of antimicrobial drugs.[21]

Treatment of presumed neonatal infections should be based on diagnostic suspicion using a thorough history and clinical examination, laboratory tests with the best sensitivity, specificity, and predictive value, and the use of deep cultures.

However, it is not always easy to implement new policies or to change physician practices. "Inappropriate practices tend to be sustained by powerful nonscientific forces,"[22] and strategies are needed to overcome administrative, traditional, educational, and patient pressures to keep performing superficial cultures.[23] Quality assurance programs are needed both in the clinical setting and in the laboratory.

Eliminating ineffective testing could reduce personnel workload in laboratory and nursery services and minimize financial costs at several administrative levels within the hospital. We encourage the further evaluation of current instruments and tests. ∎

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