DIAGNOSTIC SENSITIVITY OF SERIAL HEELSTICK BLOOD CULTURES IN NEONATAL SEPSIS

by

Josanne M. Paxton

A thesis submitted to the faculty of
The University of Utah
in partial fulfillment of the requirements for the degree of

Master of Science

College of Nursing

The University of Utah

March 1984

THE UNIVERSITY OF UTAH GRADUATE SCHOOL

SUPERVISORY COMMITTEE APPROVAL

of a thesis submitted by

Josanne M. Paxton

This thesis has been read by each member of the following supervisory committee and by majority vote has been found to be satisfactory.

Chairman: Carol A. [redacted] R.N., Ph.D.

Terry Erdman, R.N., M.S.

THE UNIVERSITY OF UTAH GRADUATE SCHOOL

FINAL READING APPROVAL

To the Graduate Council of The University of Utah:

I have read the thesis of Josanne M. Paxton in its final form and have found that (1) its format, citations, and bibliographic style are consistent and acceptable; (2) its illustrative materials including figures, tables, and charts are in place; and (3) the final manuscript is satisfactory to the Supervisory Committee and is ready for submission to the Graduate School.

2-14-84
Date

Member, Supervisory Committee

Linda K. Amos, Ed.D., F.A.A.N.
Chairman Dean

Approved for the Graduate Council

James L.
Dean of The Graduate S

ABSTRACT

The diagnosis of sepsis in the newborn is dependent on the recovery of bacterial organisms from the bloodstream. However, single blood culture results are often negative for the growth of organisms. The literature suggests that serial cultures might identify pathogens that are often missed when only a single culture is drawn. A heelstick blood culture method has been shown effective in identifying pathogenic organisms. This method would allow the clinician to draw serial cultures with less difficulty and minimal trauma to the infant.

The purpose of this study was to determine whether serial heelstick blood cultures improved sensitivity to pathogenic organisms. An initial venous culture was drawn followed by three heelstick cultures with 15-minute intervals between each draw. All venous cultures were negative for the growth of an organism. Only one heelstick culture yielded a positive result which was felt to be a contaminant since the organism was not reported on the venous or other heelstick cultures. Therefore, continued

research with a larger sample size is needed to determine whether serial heelstick blood cultures will indeed yield a higher incidence of pathogenic organisms than a single venous culture.

CONTENTS

LIST OF TABLES

ACKNOWLEDGMENTS

The author wishes to express her gratitude to all those who aided in the completion of this study.

Sincere appreciation is extended to the investigator's Supervisory Committee, Carol Kirgis, R.N., Ph.D. (Chairperson), Larry Eggert, M.D., and Terry Erdman R.N., M.S. for their assistance and ongoing support, to the nursing staff and pediatricians at the LDS Hospital Special Care Nursery for their cooperation and patience and to Dr. Gooch and the Department of Bacteriology at Primary Children's Medical Center for their active involvement in the study.

CHAPTER I

INTRODUCTION

> The neonatal host in his immaturity and new environment is susceptible to invasion and rapid spread of organisms so that septicemia with or without meningitis occurs at a rate and tempo more striking than any other period of time (Krugman, Ward & Katz, 1977, p. 194).

Bacterial organisms can appear in any of the major organ systems of its host, but are most commonly found in the blood, meninges and respiratory system. The emphasis of this review will be on septicemia, although it is not always possible to separate the site of infection.

The clinician is challenged with the task of diagnosing sepsis through the identification of maternal and neonatal risk factors and the interpretation of laboratory data. The recovery of bacterial organisms from the bloodstream is an essential aspect in the diagnosis of sepsis. In the adult, cultures are drawn at half hour intervals until a minimum of three have been obtained.

> A single negative blood culture should never be depended on to eliminate the

> possibility of bacteremia, because single specimans may be sterile even though the bloodstream as a whole is infected (Finegold & Martin, 1982, p. 43).

This is significant for the neonate who presents with clinical signs and symptoms of sepsis but in whom single blood culture results are often negative for the growth of pathogenic organisms.

Serial cultures in the infant would perhaps identify bacteremia otherwise missed when only a single blood draw has been done. However, the clinician often encounters difficulty in obtaining cultures in the neonate, especially in the large for gestational age (LGA) infant where veins lie deep underneath fatty tissue, in the extremely premature infant, and in the infant who has been hospitalized for an extended period of time and who has already had numerous venipunctures. There may also be a problem with contamination of the culture site during the procedure, especially when one has met with failure, and frustration ensues.

Due to the risk of contamination and the difficulty often encountered when attempting to draw a venous blood culture, an alternative method has been proposed in the literature. A recent study by Knudson and Alden (1980) reported the heelstick blood culture method to be effective in identifying the presence

of pathogenic organisms in the neonate suspected of sepsis. This method allows the clinician to obtain blood specimens from the neonate with less difficulty. It is now possible to draw serial blood cultures with minimal trauma to the infant and increased efficacy. The purpose of this study is to determine whether serial heelstick blood cultures improve sensitivity to pathogenic organisms in the neonate suspected of sepsis.

Problem Statement

Is there an increase in the sensitivity of blood cultures when a serial heelstick method is used to determine the presence of pathogenic organisms in the neonate suspected of sepsis?

Review of Literature

"Sepsis neonatorum is a disease of infants who are less than one month of age, are clinically ill and who have positive blood cultures" (Avery, 1981, p. 728). The incidence is about one in 1,000 of live, full-term births and four of 1,000 premature births (McCracken & Nelson, 1977). According to Daum and Smith (1979), infection accounts for approximately 10% of all neonatal deaths and, therefore, warrants further investigation.

Epidemiology

Although the incidence of sepsis has remained virtually unchanged over the past decade, the major organisms responsible for this disease have changed. The 1930s and 40s saw a high incidence of Group A Streptococcus which was then replaced by Escherichia coli as the agent responsible for the majority of infections in the mid 1940s and 50s (Wientzen & McCracken, 1977).

Staphylococcus aureus emerged during the 1950s and continued into the 1960s as a significant cause of neonatal sepsis (Avery, 1981).

Presently, the most common contributing organisms of sepsis neonatorum are Group B Streptococcus, Staphylococcus enterococcus, Lysteria monocytogens and Escherichia coli. Group B Streptococcus (GBS) and Escherichia coli (E. coli) are responsible for the majority of cases of sepsis, pneumonia and meningitis during the first week of life and account for approximately 60% of all infections in the neonate (Wientzen & McCracken, 1977). Because of their significant contribution as life threatening infections, they will be discussed in further detail.

Group B Streptococcus (GBS), a gram positive cocci, has become the most common cause of infectious

disease in the newborn period. Wientzen and McCracken (1979) evaluated the incidence of septicemia in the newborn over four years and found GBS to be responsible for 39% of the total number of infections. It is commonly found in the female genital tract with a maternal carrier rate of 30% (Daum & Smith, 1979). The organism can then be transferred via vertical transmission, that is, from mother to infant. Exposure may occur during delivery by contamination in the birth canal or in utero with entrance of the organism through ruptured membranes. Reports have shown that "infants born to Group B strep carriers are at risk for developing 'fetal distress' during labor, prematurity and sepsis/meningitis in the neonatal period" (Christensen, 1982, p. 139). However, it should be noted that for every infant colonization, only one in 100-200 ever develops the disease (Wientzen & McCracken, 1979). A number of factors appear to correlate with the presence of colonization in the mother, including a history of having sexual intercourse, presence of an intrauterine device, and in women less than 21 years old (Baker, 1977).

Both early and late onset of the BGS syndrome has been described in the literature. The early onset form of the disease usually develops during the first 6-48

hours of life indicating an intrauterine means of transmission (Christensen, 1982). The infant often has respiratory symptoms indistinguishable from respiratory distress syndrome. Other symptoms include cyanosis, tachypnea or apnea, acidosis and shock.

> Early onset disease is characterized by frequent association with maternal obstetrical complications, severe multisystem involvement and a high mortality rate (60-75%)... (Yow, 1975, p. 162).

The late onset syndrome occurs between 10 and 50 days and may present with nonspecific clinical findings. It frequently involves the meninges and has a mortality rate of 14-18% (Yow, 1975). It is thought to be of nosocomial origin due to its later onset.

> One group of investigators suggests that up to 40% of neonates who do not acquire Group B strep from the genital tract of their colonized mothers will be colonized with these agents during hospitalization in the newborn nursery (Baker, 1977, p. 144).

Escherichia coli (E. coli), a gram negative rod, is the second most common cause of sepsis neonatorum. Wientzen and McCracken (1977) found it to be responsible for 17% of neonatal sepsis. E. coli is present in the female genital tract with verticle transmission being the principle means of transfer to the newborn

(Shraff, 1975). There are approximately 200-300 colonized infants for each one who actually develops sepsis (Wientzen & McCracken, 1977). Signs and symptoms are discussed under clinical manifestations of sepsis.

In addition to maternal-infant transfer, it has been observed that nosocomial spread contributes significantly to infection in the newborn. A unique form of E. coli has been described in the literature as a syndrome of bacteremia, polynephritis and direct hyperbilirubinemia and may be confused with biliary atresia or neonatal hepatitis.

Immunological Response

Goldman has aptly described the transition from intrauterine to extrauterine life when stating that "the vast majority of term neonates weather their abrupt exposure to the diverse microbial world of the birth canal without incident" (1981, p. 417). However, the infant who is exposed to pathogens during delivery or hospitalization is at a disadvantage due to immature defense mechanisms. Immunocompetence in the newborn has been found to be related to age and postnatal immunological experience with his responses being different and less adequate than that of an adult (Mark & Welch, 1981).

The newborn's defense system includes two types

of immune reactions which are interrelated. They are antibody-mediated and cell-mediated immunity. The antibodies which play a significant role in the physiological response to sepsis include Immunoglobin G (IgG), IgA and IgM. The IgG antibody is of maternal origin and is the only one to cross the placental membrane in effective quantities. It provides protection against gram positive organisms through phagocytosis. The fetus is capable of producing IgM antibodies as early as 20 weeks gestation. However, they are not synthesized unless stimulated by antigens (Krugman et al., 1977). If IgM levels are found to be higher than normal in the neonate, one should be suspicious of the possibility of intrauterine infection, especially gram-negative organisms.

In those infants who are born prematurely, the IgG and IgM levels are lower than normal and proportional to the infant's gestational age (Clark & Affonso, 1979). This, in addition to a lower complement, places the premature infant at an increased risk for sepsis. Complement is responsible for lysis of cells and destruction of pathogenic organisms. Although the third component of complement, C_3, can be synthesized in the fetus as early as 29 days gestation, it is, in general, found in low levels in the neonate, limiting

the process of lysis and the ability of macrophage to attach to organisms (St. Geme, 1975). However, the phagocytic response to pathogens appears to enhance production of complement, indicating that the antigen stimulation may be involved in the promotion of complement synthesis. Consequently, the neonate is somewhat capable of responding to infections.

In summary, the components of the neonate's immune system are, for the most part present, but respond suboptimally in early life. Therefore, the full-term infant exposed to bacteria during delivery and/or hospitalization may not be able to respond with complete immunological mechanisms. The premature infant is placed at a further disadvantage due to ever lower levels of antibodies and complement.

Risk Factors

A number of risk factors have been identified as predisposing the neonate to sepsis. As alluded to previously, the neonate who presents with sepsis in the first few days of life has probably acquired an intrauterine infection or has been infected during delivery. Nosocomial organisms are more likely to be responsible when the infant develops an infection later on during the course of hospitalization.

Although the majority of infections among

> neonates still occur during the first few days of life and are the result of intrapartum exposure to maternal genital microorganisms, an increasing percentage of these infections have their onset beyond the age usually required for newborn hospitalization and are due to nosocomial pathogens (Baker, 1981, p. 698).

Berquist et al. (1979) report finding GBS associated with complications during pregnancy and delivery and gram negative organisms associated with surgeries and placement of catheters in the neonate.

Identification of risk factors, both maternal and neonatal, is important in that it alerts the clinician to an increased susceptibility to infection in the infant (see Table 1). Maternal factors predisposing the infant to sepsis include maternal fever, rupture of membranes greater than 24 hours, a prolonged or difficult labor and chorioamnionitis. The neonate is at additional risk if he/she is premature, low birthweight, meconium stained or asphyxiated at birth. Iatrogenic factors are also known to predispose the neonate to infection. As patient care becomes more complicated, there is an increased opportunity for the introduction of pathogenic organisms. Early recognition of these risk factors may aid the clinician in, at least transiently, diagnosing the infant who is presenting with vague, nonspecific symptoms.

Table 1

Risk Factors of Sepsis Neonatorum

Maternal Factors	Neonatal Factors
1. Poor prenatal care.	1. Low birth weight.
2. Poor nutrition.	2. Prematurity.
3. Low socioeconomic status.	3. Abnormal delivery, i.e., breech.
4. Maternal fever.	4. Birth asphyxia.
5. Chorioamnionitis.	5. Meconium staining.
6. Prom > 24°.	6. Resuscitation.
7. Prolonged or difficult labor.	7. Catheterization.
8. Premature labor.	8. Congenital heart disease or anomolies.
9. Urinary tract infection.	
10. Recurrent abortion.	

Note. Adapted from Pierog & Nigam, 1976; Daum & Smith, 1979; Mark & Welch, 1981.

Clinical Manifestation

The signs and symptoms of sepsis neonatorum have been briefly described as they pertain to GBS including the differentiation between early and late onset. Presented here are the many clinical manifestations associated with sepsis in general (see Table 2). It is apparent that these signs and symptoms are often nonspecific and subtle, often picked up by the mother or nurse who state that the infant "just isn't right." The clinician must suspect and treat a large number of infants before an absolute diagnosis is ever made.

Although the symptoms of sepsis often involve any or all organ systems, gastrointestinal manifestations are often the first to be identified. These include poor feeding, regurgitation, vomiting, anorexia, abdominal distention and diarrhea (Wientzen & McCracken, 1977). Temperature instability may also be observed, either hyperthermia or less frequently hypothermia. The septic infant may present with respiratory distress which can masquerade as hyaline membrane disease (Neonatal Bacteremia, 1971). Although most commonly associated with GBS, tachypnea, cyanosis, retractions and grunting may be seen with infections caused by any one of the many pathogens. Jaundice has been found in approximately one-third of septic infants

Table 2

Signs and Symptoms of

Sepsis Neonatorum

Signs and Symptoms	
Thermoregulation	Respiratory
Fever	Grunting
Hyperthermia	Retracting
Hypothermia	Cyanosis
	Apnea
Gastrointestinal	Tachypnea
Poor feeding	Skin
Vomiting	
Diarrhea	Rash
Abdominal distention	Pustules
Increasing residuals	Jaundice
Hepatomegaly	Pallor
	Vasomotor instability
Neurological	
	Cardiovascular
Lethargy	
Jitteriness	Tachycardia
Irritability	Arrythmias
Seizures	Hypo/Hypertension
Hypotonia/Hypertonia	Cold/clammy
Bulging fontanells	Decreased peripheral perfusion

Note. Adapted from Wientzen & McCracken, 1977; Spector, Tricknor & Grossman, 1981.

suggesting that sepsis be considered when encountering unexplained pathological jaundice (Wientzen & McCracken, 1977).

Cruz and associates have identified the most common symptoms of sepsis as

> alterations of body temperature (most frequently hyperthermia), gastro-intestinal alterations (food refusal, vomiting, diarrhea, weight loss), hepatoslenomegaly, jaundice, neuromuscular alterations (convulsions, muscular tone alterations) and respiratory distress (cyanosis, apnea) (1979, p. 13).

Should any of these be encountered in an infant, especially with significant maternal and/or neonatal risk factors, a high index of suspicion should be aroused. Late onset and often fatal symptoms of sepsis include shock, convulsions and bleeding disorders.

Laboratory Aids

There are a number of hematological changes which may strongly suggest sepsis in the newborn, although they are of limited value in the absolute diagnosis of septicemia (refer to Table 3). Included are IgM concentrations in the cord blood and C-reactive protein, an acute phase reactant present in the blood during inflammatory conditions. Alder and Denton (1975) investigated the usefulness of the erythrocyte sedimentation rate (ESR) in the neonate. It is a nonspecific

Table 3

Laboratory Aids in Diagnosing Sepsis

Laboratory Aids	Significant Data
WBC	$<5,000/mm^3$ or $\triangleq$ $20,000/mm^3$
Absolute neutrophil count	Abnormally high or low counts (refer to Manroe)
Ratio of immature to total neutrophils (I/T ratio)	>0.3
IgM	Elevation of > 20 mg/dl
Erythrocyte sedimentation rate (ESR)	Ranges between >1/mm/1h at 12° of age to 17/mm/1h at 14 days of age
C-reactive protein	> 2 mg/dl may be elevated in first 48°

Note. Adapted from Alder & Denton, 1975; Spector et al., 1980; Manroe, 1979.

test of tissue damage known to be evaluated during infection. They reported that infants who were infected had marked elevations in the ESR and found the test useful in evaluating newborns with possible sepsis.

The white blood count and differential have been widely investigated for their usefulness in the diagnosis of infection. Spector et al. (1981) found that a white blood count less than 10,000/mm^3 greater than 20,000/mm^3 to be strongly suggestive of sepsis. However, others find the white blood count to be of limited value as a diagnostic tool.

Manroe (1979) evaluated neutrophil counts including total neutrophils, immature neutrophils and the proportion of immature to total neutrophils. "Of the infant's studied, neutropenia was the single most accurate predictor of infection..." (Manroe, 1979, p. 95). In addition, an elevated ratio of immature to total neutrophils was also found to be significant.

It is recommended that bacteriologic studies, hematologic studies and clinical evaluation all be used to aid in the identification of infants with possible bacterial infections. Although there are a number of laboratory aids which may strongly suggest sepsis, an absolute diagnosis is made only with the

recovery of the organism. In those infants suspected of sepsis or meningitis, blood, urine and cerebral spinal fluid are cultured prior to the initiation of antimicrobial therapy. When the prenatal history or physical exam arouse suspicion, but infection is unlikely, blood and urine cultures are usually sufficient (Wientzen & McCracken, 1977). Because the neonate has a limited ability to respond to bacterial pathogens, suspected infection requires prompt initiation of antimicrobial agents.

Blood Cultures

Congruency in the literature concerning appropriate sites for obtaining blood cultures in the neonate is lacking. According to Wientzen and McCracken (1977, p. 35), "there are three sites for sampling blood for cultures that may give reliable results: peripheral vein, umbilical artery and capillaries." The most accepted practice is to draw blood for cultures from a peripheral vein. In 1976, Cowett, Peter, Hakason and Oh evaluated the reliability of blood cultures obtained from an umbilical artery catheter. Their results showed a close correlation between the cultures drawn by venipuncture and those obtained from a catheter during the first nine hours of life. Current literature states that cultures can be drawn

from the umbilical catheter if done immediately after placement (Cloherty & Stark, 1980; Daum & Smith, 1979).

A method of capillary blood cultures drawn from the big toe was first investigated by Holt, Frankcombe and Newman in 1974. Although comparison was not made with simultaneous venous drawings, results showed a lower contamination rate in the capillary (4.6%) versus the venous cultures (7.5%). In 1977, Mangurten and LeBeau evaluated the diagnosis of neonatal bacteremia by a microblood culture technique in 195 infants. Blood was obtained from the outer border of the heel and simultaneously from a peripheral vein. Their conclusion was that "the microblood cultures were reliable in approximately 73% of instances and possibly in 100% of instances if contamination of the venous specimen is considered" (p. 991). However, it was suggested that blood still be drawn from a peripheral vein for comparative purposes if obtaining blood by heelstick.

In 1980, Knudson and Alden published data on neonatal heelstick blood cultures and use of a micromethod. They evaluated the use of 0.2 ml of capillary blood as compared to a simultaneous draw of 0.5 - 1.0 ml of venous blood. They obtained a total of 50 paired blood cultures. Eight of their infants had identical

organisms growing in both the heelstick and venous cultures. An additional three had positive heelstick cultures while the venous cultures were negative. However, a culture of peritoneal fluid in these infants during surgery, produced the same organisms as was found in the heelstick culture. In none of their samples were the venous cultures positive and the heelstick cultures negative. Their conclusion was that "small volume blood cultures obtained from a heelstick are as sensitive as those obtained from venous sites" (p. 507).

There is also dispute over the number of cultures which should be drawn on an infant suspected of sepsis. A study by Franciosi and Favara (1972, p. 217) determined that "a single blood culture was satisfactory for confirming the diagnosis of septicemia..." However, other researchers have suggested drawing two or more cultures obtained from different sites (Moffet, 1975; Finegold & Martin, 1982). Hosmer and Sprunt (1972) evaluated cultures of cord blood, gastric aspirate and infant blood drawn on infants born of mothers with prematurely ruptured membranes. They found culture from cord blood and gastric aspirate to be inefficient as a screening method for sepsis. Their recommendation was that two or more blood cultures be obtained from

different sites to minimize debate over findings.

Hypotheses

The two hypotheses tested in this study were:

1. The heelstick method is as sensitive a determinant of sepsis neonatorum as are cultures obtained from a venous site.

2. Serial heelstick blood cultures will yield a higher incidence of positive results due to pathogenic organisms than is found in a single initial venous blood culture.

Definitions

Sepsis Neonatorum

Sepsis neonatorum is defined as an illness of newborns who present with the clinical symptoms of the disease and who have positive blood cultures.

Peripheral Blood Cultures

Peripheral blood cultures are the standard method of blood withdrawal by venipuncture to determine the growth of bacterial organisms in the blood.

Heelstick Blood Cultures

Heelstick blood cultures are defined as a method of blood withdrawal taken from the heel to determine the growth of bacterial organisms in the blood stream.

Assumptions

Three basic assumptions have been made in developing this study:

1. Peripheral blood cultures are a reliable method for determining the presence of pathogenic organisms in the bloodstream.

2. There is no significant difference in the incidence of false positive results due to contamination in those cultures drawn by the heelstick method as compared with those drawn by venipuncture.

3. Not all infants on whom cultures are drawn will be positive for sepsis.

CHAPTER II

METHODOLOGY

Design

A quasiexperimental design was used to test the hypotheses of this study. The important components of this experimental design are manipulation of the independent variable and, either the use of a control group or assignment of subjects on a random basis (Polit & Hungler, 1978). This study allowed for the manipulation of the independent variable and the use of each subject as his or her own control (X_1: X_2 X_3 X_4). A threat to external validity did exist since there was no random selection of subjects from the general population.

The equivalent time-samples design controls for all threats to internal validity including history, selection, mortality and instrumentation. In addition, the strength of the design increases when there is increased repetition of treatments (Campbell & Stanley, 1963). In this study, each

infant had an initial venous blood culture drawn followed by a total of three serial heelstick blood cultures. The independent variable has been identified as the heelstick method of blood withdrawal and the culture drawn by venipuncture as a control. The dependent variable is the result of the heelstick blood cultures.

Limitations

Limitations to the design of this study have been identified. An attempt was made to control for threats to instrumentation by having all blood cultures drawn by the investigator. Consequently, a smaller sample size was obtained. Physicians and/or staff nurses were relied upon to contact and inform the researcher of any infants requiring blood cultures, which was forgotten at times. In addition, the investigator was not always available. As a result, infants were missed and the potential sample size was reduced.

A second limitation to the study was the absence of positive blood culture results. This was probably secondary to the small sample size.

Subjects

The target population is defined as "the total group of subjects about whom the investigation is

interested and to whom the results could reasonably by generalized" (Polit & Hungler, 1978, p. 260). The target population of this study included all neonates who required blood cultures because of suspected sepsis. The subjects for this study, or the accessible population, were infants in the Special Care Nursery at LDS Hospital in Salt Lake City, Utah. Heelstick blood cultures were drawn on any neonates who had peripheral blood cultures ordered by his or her physician. Because all infants, regardless of gestational age, weight, or length of hospitalization who are suspected of sepsis are at risk, no constraints were placed on the inclusion of subjects.

The following criteria were used to identify those infants who required blood cultures drawn:

1. The infant with maternal or neonatal risk factors which place them at increased risk for infection (Table 1).

2. The infant with the clinical signs and symptoms of sepsis (Table 2).

3. The infant with laboratory data strongly suggestive of sepsis (Table 3).

Instrumentation and Procedures

A method for drawing heelstick blood cultures was designed for the LDS Hospital Nursery (Appendix

A). The equipment needed to draw blood could be found on the neonatal heelstick blood culture tray and included one lancet, one caraway tube, one #2 needle, one millipore filter with rubber tubing, and two Providone iodine swab sticks. The procedure was carried out wearing sterile gloves to reduce the risk of contamination. A lancet was used to puncture the heel after it had been cleaned for one minute with the swab sticks. The excess preparation was removed with sterile gauze. Blood was then drawn into the caraway tubes until it was half full, equaling 0.25 ml. After attaching the millipore filter to the collecting end of the caraway tube, a sterile needle was attached to the opposite end and the blood was placed in a culture bottle which had been cleaned with Betadine and wiped with a sterile gauze. Pediatric blood culture bottles containing columbia broth and manufactured by Gibco Laboratories were used in this investigation.

This procedure was repeated an additional two times with 15 minute intervals between each draw. Infants suspected of sepsis are often at risk for other problems and usually require multiple lab work to be done. All attempts were made to incorporate the serial blood culture draws with other required lab work (i.e., Dextrostix®, CBC, capillary blood gas),

in order to reduce any undue stress on the infants. If the attending physician felt that the infant might be harmed by delaying antibiotics one hour, the infant could be excluded from the study.

A venous sample was also collected at the same time as the first heelstick culture (Appendix B). A venous site was identified and cleaned with Betadine for one minute. The site was then wiped with sterile gauze. The venipuncture was performed and between 0.5 and 1.0 ml of blood was obtained and placed in a prepared culture bottle. Pressure was applied at the venipuncture site until bleeding stopped.

CHAPTER III

RESULTS AND DISCUSSION

Blood cultures were reported as either positive or negative for the growth of an organism. Nonparametric tests can be used with ordinal data and do not require stringent assumptions concerning the nature of the population. A specific test was needed to establish the efficacy of serial heelstick blood cultures as compared with a single venous culture. The Sign Test met all criteria and was used to determine whether a statistically significant difference existed between related samples (Knapp, 1978).

For this study, positive cultures were assigned a value of one and negative cultures a value of zero. Heelstick samples were analyzed in relation to the venous sample. The differences between samples were expressed as "+" and "-" values (Figure 2). If the value of both venous and heelstick cultures were equal, the pair was dropped from the analysis.

The null hypothesis was tested by obtaining a critical value from a sign test table. "The value

Subject	Venous	H.S.1	Sign
1	1	0	+
2	0	1	-
3	0	1	-

Figure 2. Sample of sign test analysis.

from this table specified the maximum number of differences in the minority direction (whichever sign is the smallest) that can occur if Ho is to be rejected" (Knapp, 1978, p. 188). If the number of "+" and "-" signs are equal, there is no difference between the groups.

Demographic Data

Data for this study were gathered from November 1982 to February 1983. Twenty-five serial cultures were obtained on 24 subjects. The demographic data collected included sex, gestational age, age when cultures drawn and reason for a septic workup. Table 4 provides this information on each infant.

Demographic observations are summarized in Table 5. Of the 25 cultures, 12 were drawn from female infants and 13 from male infants. The mean gestational age of the subjects was 36.8 weeks. Eighty percent of the cultures were drawn within the first day of life. Two of the infants, who were hospitalized for an extended period of time, presented with a late onset of symptoms. Late onset syndrome usually occurs between 10 and 50 days, manifested by nonspecific clinical findings, and is usually thought to be of nosocomial origin.

A neutrophil count was also calculated for all

Table 4

Demographic Data

Subject	Diagnosis	Sex	Gestational Age	Age When Cultures Drawn
1	TTN vs Aspiration Pneumonia	M	37 wks	5°
2	Meconiom Aspiration	F	42 wks	3°
3	Apnea with questionable etiology	F	40 wks	18°
4	Elevated temperature	F	40 wks	46°
5	Respiratory arrest at delivery	M	41 wks	2°
6	Maternal temperature	M	35 wks	1°
7	Maternal temperature	F	41 wks	2°
8	PROM x 14 days	M	32 wks	2°
9	Meconium aspiration	M	37 wks	2°
10	Prematurity	F	31 wks	408°
11	Maternal temperature	M	41 wks	3°
12	Respiratory distress	M	35 wks	4°
13	PROM	M	39 wks	26°
14	-	M	40 wks	5°
15	Aspiration vs infection	F	39 wks	8°
16	RDS vs pneumonia	F	38 wks	5°
17	Probable RDS	M	35 wks	5°
18	-	M	40 wks	1°
19	Maternal fever	M	36 wks	1°
20	Increased FiO_2 requirements	F	27 wks	792°
21	Staph epidermis from tip of percutaneous	F	27 wks	840°
22	Prematurity	F	35 wks	12°
23	C-section for toxemia	F	37 wks	17°

Table 4 Continued

Subject	Diagnosis	Sex	Gestational Age	Age When Cultures Drawn
24	Respiratory arrest at delivery	M	39 wks	2°
25	Pneumonia vs RDS	F	36 wks	14°

Note. ° = hours; PROM = premature rupture of membranes.

Table 5

Demographic Observations

Observations
1. 12 infants were female and 13 infants were male.
2. 80% of the cultures were drawn within the 1st day of life.
3. Mean gestational age was 36.8 weeks.
4. 8% of the neutrophil counts were significantly decreased.

the infants but one. The recovery of an organism via blood cultures is the only means by which an absolute diagnosis of sepsis is made. However, hematologic studies continue to aid in the identification of infants suspected of sepsis. Of these studies, neutropenia in the presence of respiratory distress is found to be the most accurate in producing septicemia. Only one subject, on whom two white counts had been drawn, was found to be neutropenic (Table 6). According to Manroe,

> Neutropenia was observed in only four clinical situations other than sepsis: maternal hypertension, confirmed periventricular hemorrhage, severe asphyxia and reticulocytosis occurring after 14 days postnatal age (1979, p. 94).

Reticulocytosis was probably the cause of neutropenia in the identified subject and not septicemia. These findings are also consistent with blood culture results.

Hypothesis One

The Sign Test was used for analysis of the first hypothesis which states that heelstick blood cultures are as sensitive a determinant of sepsis as are venous cultures. However, all the venous cultures in this study were negative for the growth of pathogenic organisms. Consequently, it was not possible to evaluate the sensitivity of heelstick cultures. Hypothesis

Table 6

Subjects' Neutrophil Counts

and Interpretation

Subject	Neutrophil count/mm^3	Interpretation[a]
1	--	--
2	12,300	elevated
3	22,000	elevated
4	18,300	elevated
5	7,500	normal
6	6,900	normal
7	20,000	elevated
8	7,300	normal
9	13,000	elevated
10	8,700	elevated
11	11,900	elevated
12	18,300	elevated
13	14,700	elevated
14	16,700	elevated
15	27,000	elevated
16	29,100	elevated
17	16,600	elevated
18	5,800	normal
19	3,700	normal
20	960	decreased
21	1,300	decreased
22	24,000	elevated
23	15,000	elevated
24	15,000	elevated
25	9,200	normal

Note. [a]Adapted from Manroe, 1979.

one was neither supported nor rejected due to insufficient data. Failure to obtain any positive venous blood cultures was probably a result of the small sample size. In addition, most infants who have risk factors and/or signs and symptoms of sepsis have negative blood cultures.

Knudson and Alden (1980) were able to determine that cultures obtained by heelstick were as sensitive as those obtained by venipuncture. Of 50 paired blood cultures, eight had identical organisms in both the heelstick and venous samples. None of their venous cultures were positive with concomitant negative heelstick cultures.

It is currently recommended that blood cultures be drawn by venipuncture. However, further evaluation of heelstick blood cultures may result in additional support of this alternative method. The clinician may then depend on a less difficult yet reliable means by which to draw blood cultures from the neonate suspected of sepsis.

Hypothesis Two

The Sign Test was used for analysis of the second hypothesis which states that serial blood cultures will yield a higher incidence of positive results due to pathogenic organisms than is found in a single

venous blood culture. All of the venous cultures in this study were negative for the growth of pathogenic organisms. One of the heelstick cultures had a positive result. When these data were subjected to analysis, no statistical differences were found at the .05 level of significance.

Therefore, the hypothesis was not supported by the data. The results of this investigation were limited by the small sample size and failure to obtain any positive venous cultures. However, the literature recommends that two or more cultures may provide more information than a single culture (Finegold & Martin, 1982; Remington & Klein, 1983). Moffet suggests that

> more than one specimen of blood should be obtained when bacteremia is suspected, and that bacteremia is sometimes missed by a single blood culture (1975, p. 368).

Further investigation involving serial heelstick blood cultures is necessary to determine whether this method will indeed yield a higher incidence of pathogenic organisms than a single venous culture.

Additional Findings

There is an ongoing debate concerning the evaluation of blood cultures when they are positive for organisms which may be contaminants versus pathogens. Positive blood culture results may in fact, be due to contami-

nation. The organism Staphylococcus epidermis (S. epidermis) is an example of such an organism. Subject #20 had a positive heelstick blood culture for S. epidermis. Although usually found in the skin and mucus membranes in humans, it can also be a pathogen (Finegold & Martin, 1982). How does one determine whether this organism is actually a pathogen or only a contaminant?

It has been recommended that two or more cultures be drawn in order to minimize this debate (Hosmer & Sprunt, 1972). However, it is often difficult to obtain one, much less multiple, venous specimens for this purpose. Serial heelstick blood cultures may prove beneficial in resolving the conflict. One may conclude in this study, that the organism S. epidermis was in fact a contaminant since it was not replicated in the venous or other heelstick cultures. The clinician may then feel safer in assuming that a particular organism is a contaminant versus a pathogen.

CHAPTER IV

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS

Summary

The purpose of this study was to determine whether serial heelstick blood cultures improved sensitivity to pathogenic organisms in the neonate suspected of sepsis. It was believed that serial cultures would perhaps identify bacteremia that is often missed when only a single draw is done. A heelstick method was used in order to reduce the difficulties encountered when attempting to draw venous blood.

Research has shown the heelstick draw to be an effective method in identifying pathogenic organisms in the blood. However, there is dispute over the number of cultures which should be drawn. Though some investigators state that a single blood culture is satisfactory, others recommend that two or more cultures be obtained from different sites. The goal of this study was to gather data which would support the use of serial blood cultures to diagnose sepsis

in the newborn.

Subjects for this study were newborns in the Special Care Nursery at LDS Hospital in Salt Lake City. Heelstick cultures were drawn on any infant who had peripheral blood cultures ordered. Each infant had a venous blood culture drawn followed by three heelstick cultures with fifteen minute intervals between each draw.

The first hypothesis stated that heelstick blood cultures are as sensitive a determinant of sepsis as are venous cultures. Since all the venous cultures were negative for the growth of an organism, it was not possible to evaluate the sensitivity of heelstick culture. Consequently, hypothesis one was neither supported nor rejected due to insufficient data.

The second hypothesis stated that serial blood cultures would yield a higher incidence of positive results than is found in a single venous blood culture. All venous cultures were negative with one positive heelstick blood culture. When the data were subjected to analysis no statistical difference existed, therefore, the hypothesis was not supported.

Conclusions

The data collected from this study were insufficient to support hypotheses one or two. Failure

to obtain any positive venous blood cultures was probably a result of the small sample size. However, earlier investigations have found heelstick cultures to be as sensitive as those obtained by venipuncture. Furthermore, the literature suggests that two or more cultures may provide more information than a single culture. Continued research with a larger sample size is needed to determine whether heelstick cultures provide this information in diagnosing sepsis in the newborn.

Recommendations

1. A larger sample size would provide better representation of the entire population and might increase the probability of obtaining positive blood culture results.

2. A minimum of 25 positive blood cultures could provide the data needed to determine whether serial heelstick cultures diagnose bacteremia more frequently than a single venipuncture.

3. By increasing the number of investigators involved in the study, a larger sample size might be obtained. However, careful instruction concerning the procedure is needed to control for threats to instrumentation.

APPENDIX A

HEELSTICK BLOOD CULTURE PROTOCOL

LDS HOSPITAL*

Nursery

Purpose: To obtain heelstick blood specimen for blood culture.

Indications:
1. To rule out possible sepsis. Usually done as part of septic workup.
2. To be used when venipuncture cannot be obtained.
3. To be used in preference to venipuncture when ordered.

Equipment: Sterile gloves

Neonatal Heelstick Blood Culture Tray (obtain from Central Supply). Includes:

- 2 Blood culture bottles
- 2 Caraway tubes
- 2 #20 needles
- 2 Millipore filters with rubber tubing
- 1 Long point lancet
- 2 Povidone - Iodine Swab Sticks
- 3 4x4 gauze dressings

Alcohol Prep
Jr. Bandaid

Method	Key Points
1. Obtain Neonatal Heelstick Blood Culture Tray from Central Supply.	
2. Open gloves and outer tray cover using sterile technique.	2. Use inner side of tray cover as sterile field.
3. Put on sterile gloves.	
4. Open Iodine Swab Sticks.	

*Reprinted with permission of LDS Hospital.

Method	Key Points
5. Holding infant's foot in left hand, prep heel with Iodine Swab Sticks for one minute.	5. Friction increases effectiveness of prep. Use careful technique on keeping right hand sterile.
6. Remove excess prep with sterile gauze.	
7. Puncture heel with lancet.	7. See Heelstick Procedure.
8. Fill both caraway tubes ½ full.	8. ½ caraway tube is .25 ml.
9. Attach rubber tubing with connecting Millipore filter to collecting end of caraway tube.	
10. Attach sterile needle to the opposite end of caraway tube.	
11. Bend tubing to slow amount of air introduced.	
12. Insert needle into blood culture bottle.	12. Vacuum pulls specimen into bottle. Millipore filter may prevent introduction of bacteria from air into the specimen.
13. Obtain .25 cc blood for each bottle.	13. Two bottles are needed. Insert needle into each bottle filling .25 cc blood in each.
14. Clean off excess iodine prep with alcohol prep and apply Bandaid.	
15. Discard supplies into proper receptacle.	

Method	Key Points
16. Chart procedure, how tolerated and any problems on flow sheet.	
17. Stamp and fill out bacteriology slip: date, time of specimen collection, diagnosis, any antibiotics currently being given, type of study requested and sign name.	
18. Attach completed labels (stamped with addressograph and "Heelstick Blood Culture" written on label) to culture bottles and place with bacteriology slip.	
19. Send labeled specimens with stamped slip to lab immediately.	19. a. Specimens for culture cannot sit at room temperature. Should go to lab as soon as possible. b. 0800-2300 may be taken immediately to Bacteriology by paging messenger. c. 2300-0800 AM nurses or designate takes to 7 East Lab and checks with night technician. If technician is not in Lab, page supervisor.

Carol Bush, RN, MS
Assistant Administrator/Nursing

April, 1980

APPENDIX B

NURSING PROCEDURE SPECIAL CARE NURSERIES: BLOOD CULTURE

LDS HOSPITAL *

Blood Cultures

Purpose: Drawing blood for diagnostic procedures.

Policy: Order by physician as part of septic workup.

Equipment:
23 or 25 gauge butterfly needle
Additional straight needle
3 gauze pads (2x2)
Betadine solution
Alcohol preps
Syringe - 3 cc
Culture media bottle
Tourniquet (rubber band)
Heat lamp if indicated
Bacteriology lab slip

Method	Key Point
1. Prepare Bacteriology requisition.	1. Complete date, time of specimen collection, diagnosis, any antibiotics currently being given, type of study desired and sign name.
2. Assemble and prepare equipment.	
3. Place heat lamp over incubator door, crib or counter top.	3. Maintains infant temperature.
4. Wipe top of culture media bottle with Betadine.	4. Allows time to dry before using.
5. Prepare infant by sliding infant's bed out of incubator or place infant on counter under heat lamp.	

*Reprinted with permission of LDS Hospital.

Method	Key Point
6. Identify and prepare site by wiping with Betadine. Allow Betadine to dry then wipe with gauze.	
7. Perform venipuncture.	7. See venipuncture procedure.
8. Apply pressure to venipuncture site using a dry sterile sponge until bleeding stops after specimen is obtained.	8. If infant is receiving heparin, maintain pressure for 5-10 minutes to control and stop bleeding.
9. Wipe away excess betadine from venipuncture area and return baby to crib or incubator.	
10. Change needle on syringe containing blood specimen.	
11. Wipe top of culture bottle with betadine and then alcohol before injecting blood into bottle.	11. Allow ample time for Betadine to dry before using alcohol.
12. Give labeled specimen with stamped slip to lab.	12. a. 8:00 a.m. - 6:30 p.m. May be taken to Bacteriology by messenger. b. 6:30 p.m. - 11:30 p.m. Messenger will take to East Lab and receptionist will place in incubator. c. 11:30 p.m. - 8:00 a.m. Nurse or designate takes to 7-East Lab and gives to night technician. If tech-

Method	Key Point
	nician is not in lab, page supervisor. d. If Bacteriology is closed, specimen is taken to 7-East Lab.
13. Chart procedure and how procedure was tolerated on flow chart.	

Sally Doshier, R.N.
Head Nurse, Special Care Nurseries

Larry D. Eggert, M.D.
Director, Newborn Services

Esther Anderson, C.N.M., M.S.
Assistant Director of Nursing

Revised from U of U NBICU May 1978
Revised October 1980
Revised December 1981
Reviewed January 1982

REFERENCES

Adler, S.M. & Denton, R.L. (1975). The erythrocyte sedimentation rate in the newborn period. The Journal of Pediatrics, 86, 942-948.

Avery, G.B. (1981). Neonatology, pathophysiology and management in the newborn. Philadelphia: J.B. Lippincott Co.

Baker, C.J. (1981). Nosocomial septicemia and meningitis in neonates. The American Journal of Medicine, 70, 698-701.

Baker, C.J. (1977). Summary of the workshop on perinatal infections due to group B streptococcus. The Journal of Infectious Disease, 136, 137-152.

Berquist, G., Eriksson, H. & Zetterstrom, R. (1979). Neonatal septicemia and perinatal risk factors. Acta Paediatrica Scandinavica, 68, 337-339.

Campbell, D.T. & Stanley, J.C. (1963). Experimental and quasiexperimental designs for research. Boston: Houghton Mifflin Co.

Christensen, K. (1982). The clinical significance of group B streptococci. The Journal of Perinatal Medicine, 10, 133-146.

Clark, A. & Affonso, D. (1979). Childbearing: A nursing perspective. Philadelphia: F.A. Davis Co.

Cloherty, J.P. & Stark, A.R. (1980). Manual of neonatal care. Boston: Little, Brown & Co.

Cowett, R.M., Peter, G., Hakason, D. & Oh, W. (1976). Reliability of bacterial cultures of blood obtained from an umbilical catheter. Journal of Pediatrics, 88, 1035-1036.

Cruz, M., Eddy, L., Figueras, J. & Jimenez, R. (1979). Neonatal sepsis, Paediatrician, 8, 4-16.

Daum, R.S. & Smith, A.L. (1979). Bacterial sepsis in the newborn. Clinical Obstetrics and Gynecology, 22, 385-409.

Finegold, S.M. & Martin, W.J. (1982). Diagnostic Microbiology. St. Louis: C.V. Mosby Co.

Franciosi, R.H. & Favara, B.E. (1972). A single blood culture for confirmation of the diagnosis of neonatal septicemia. American Journal of Clinical Pathology, 57, 215-219.

Goldman, D.A. (1981). Bacterial colonization and infection in the neonate. The American Journal of Medicine, 70, 417-422.

Holt, R.J., Frankcombe, C.H. & Newman, R.L. (1974). Capillary blood cultures. Archives of Diseases in Children, 49, 318-321.

Hosmer, M.E. & Sprunt, K. (1972). Screening method for identification of infected infants following premature rupture of maternal membranes. Pediatrics, 49, 283-285.

Knapp, R.G. (1978). Basic statistics for nurses. New York: John Wiley & Sons.

Knudson, R.P. & Alden, E.R. (1980). Neonatal heelstick blood culture. Pediatrics, 65, 505-507.

Krugman, S., Ward, R. & Katz, S. (1977). Infectious diseases of children. St. Louis: The C.V. Mosby Co.

Mangurten, H.H. & LeBeau, L.J. (1977). Diagnosis of neonatal bacteremia by a microblood culture technique. The Journal of Pediatrics, 90, 990-992.

Manroe, B.L. (1979). The neonatal blood count in health and disease. The Journal of Pediatrics, 95, 89-98.

Mark, M.I. & Welch, D.F. (1981). Diagnosing bacterial infections of the newborn infant. Clinics in Perinatology, 8, 537-558.

McCracken, G.H. & Nelson, J.D. (1977). Antimicrobial therapy for newborns. New York: Grune & Stratton.

Moffet, H.L. (1975). Pediatric infectious diseases. Philadelphia: J.B. Lippincott Co.

Neonatal bacteremia: Diagnosis and management. (1971). British Medical Journal, 1385-1386.

Pierog, S. & Nigam, S. (1976). Neonatal sepsis. Pediatric Annals, 5, 98-106.

Polit, D. & Hungler, B. (1978). Nursing research: Principles and methods. Philadelphia: J.B. Lippincott Co.

Remington, J.S. & Klein, J.O. (1983). Infectious diseases of the fetus and newborn infant. Philadelphia: W.B. Saunders Co.

Shraff, L.D. (1975). Epidemiology of Escherichia coli K in healthy and diseased newborns. The Lancet, 1, 1099-1104.

Spector, S.A., Ticknor, W. & Grossman, M. (1981). Study of the usefulness of clinical and hemotological findings in the diagnosis of neonatal bacterial infections. Clinical Pediatrics, 20, 385-392.

St. Geme, J.W. (1975). Perinatal and neonatal infections. The Western Journal of Medicine, 122, 359-366.

Wientzen, R.L. & McCracken, G.H. (1977). Current problems in pediatrics, 8, 3-61.

Yow, M.D. (1975). Epidemiology of group B streptococcal infections. In S. Krugman & A. Gershon (eds.), Infections of the fetus and newborn, 3, New York: Allen R. Liss, Inc.