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Early Diagnosis and Treatment of Neonatal Sepsis

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Abstract. Perinatally acquired bacterial neonatal sepsis is a low incidence, high risk disease with a relatively benign treatment. Accurate diagnosis is difficult because there is no definitive diagnostic test; even blood cultures have an unacceptably low sensitivity. Therefore, the clinician must accept that a number of neonates who do not have the disease will have treatment initiated for sepsis. In order to treat rapidly all infants with sepsis and to minimize therapy for those without infection, historical, clinical, and laboratory data can be used together in a management approach to achieve optimal results. A systemized approach using history, examination, sepsis screen laboratory tests, and cultures is presented to guide clinical management. **(Indian J Pediatr 1998; 65 : 63-78)**

Key words : *Bacterial sepsis; Blood cultures; Low sensitivity.*

The early and efficient diagnosis of neonatal bacterial sepsis remains a difficult task. To delay treatment until signs and symptoms of sepsis are obvious brings the risk of preventable mortality, yet to treat neonates with antibiotics presumptively on the basis of subtle signs or risk factors alone is likely to result in over treatment. The problem is that neonatal sepsis is a disease that may start with minimal or nonspecific symptoms and has a relatively low incidence (1 to 8 cases/1000 live births)[1-3], yet a high risk of mortality (approximately 25%)[1,3-5]. Because the treatment is benign relative to this "low incidence, high risk" disease and babies who develop sepsis often die rapidly, clinical practice has evolved such that many more babies are evaluated and treated for sepsis than actually have the conditions. It is estimated that between 11 and 23 noninfected newborns are treated in intensive care nurseries for every one with documented infection[4,6,7]. Although this approach is reasonable given the dire outcome of a missed diagnosis, improvement in our diagnostic accuracy should diminish exposure to the risks of unwarranted antibiotic therapy such as alteration in normal flora[8,9], medication errors[10], intravenous infiltrates, and excessive financial and emotional cost to the parents. The goals of the clinician are to : (a) develop a systematic diagnostic approach of neonatal sepsis based on the relative importance of the known symptoms and risk factors, (b) miss no cases–this will require some "over treatment" of newborns in the identified high-risk group, (c) institute effective antimicrobial and supportive treatments, (d) minimize duration of therapy for those high-risk infants who prove to be

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uninfected, and (e) provide a safe observation protocol for the low-risk neonate. Unless otherwise specified, the discussion is limited to the diagnosis of perinatally acquired sepsis during the first week of life.

HISTORICAL AND PREDISPOSING RISK FACTORS

Because of the danger of delayed diagnosis, clinicians must pay careful attention to the perinatal history in order to assess the risk of sepsis in a newborn infant and also the single and additive risks for various historical factors in order to have a rational approach to patient management. These historical factors should raise the suspicion of possible infection. Asymptomatic neonates with risk factors should be carefully observed and screened. Infants with symptoms such as respiratory distress are more likely to have sepsis rather than other respiratory conditions if risk factors are present. Table 1 shows the highly suspected sepsis group infants with negative culture results but highly probable bacterial infection, such as those with pneumonia. The rate of proven plus highly suspected infections seems to be approximately twice the culture-proven rate[11,12]. Group B Streptococcus (GBS) is the most common etiology of neonatal sepsis in the USA, but the incidence of GBS colonization and infection in India is quite low. However, the pathophysiology of GBS infection is of academic interest, and may have relevance to other neonatal pathogens.

Prolonged Rupture of Membranes and Chorioamnionitis

Both the multicenter collaborative perinatal project of the National Institute of Neurological and Communicative Disorders and Stroke[13] and studies by St. Geme *et al*[12] concluded that the incidence of documented sepsis in neonates born to mothers with rupture of membranes for more than 24 hours is approximately 1%. When signs and symptoms of chorioamnionitis are present the risk of proven sepsis increases to 3–5%. Unfortunately the clinical diagnosis of chorioamnionitis may be difficult to confirm, but should be suspected in the presence of maternal fever (>100.4°C), uterine tenderness, purulent or foul-smelling amniotic fluid, or fetal tachycardia. The placental pathologic diagnosis is easy to make, but the result is rarely known in time to influence clinical management. There is only a weak correlation between the pathologic findings of chorioamnionitis and sepsis in the infant[14].

Maternal Colonization with Group B Streptococcus

Maternal colonization with GBS without clinical complications carries a 0.5–1% risk of neonatal sepsis[15-17], similar to the risk of uncomplicated PROM. Boyer and Gotoff's comprehensive studies have identified three high risk situations that increase the likelihood of neonatal GBS disease when the mother is colonized : (a) PROM > 18 h (risk increased seven fold), (b) maternal fever (risk increased four fold), and (c) prematurity (risk increased seven fold)[18].

The density of maternal and neonatal GBS colonization is an infrequently quantified but potentially important determinant of the risk of invasive disease. Dillon *et al*[17] defined heavy neonatal GBS colonization as recovery of GBS from three to four external sites, and light colonization from one to two sites only. Neonates with heavy coloni-

zation had an attack rate of 5%, compared to 0.4% in those lightly colonized. Similar findings were reported by Pass *et al*[19]. Light colonization may still lead to infection, when accompanied by PROM[20]. Twin gestations may be at increased risk for GBS sepsis even when corrected for prematurity[21,22]. A major limitation of our ability to manage GBS infections postnatally is that the majority of the early-onset disease cases are acquired in utero[23,24]; antenatal diagnosis and treatment are required to fully control early-onset GBS disease.

Prematurity

Inherent in the preterm neonate are deficiencies in most arms of the immune system, including immunoglobulin production, complement opsonic functions, and phagocytic capability[25]. As noted above, the risk of GBS sepsis is increased markedly in the preterm neonate. Following PROM, the risk of infection in the preterm infant is 8-11 times that of the term infant. These infants exhibit an attack rate that ranges from 4% to 11%[12,26].

Perinatal Asphyxia

In a study by St. Geme *et al*[12] a 5-min Apgar score <6 in the presence of PROM was as strong a predictor of neonatal sepsis as chorioamnionitis. Similarly, a Danish study found that 27% of preterm infants with PROM and perinatal asphyxia has proven sepsis[27]. Clinical judgement is required to rule out other obstetric causes of asphyxia, which may not be due to infection.

Male Gender

Observations from 30 years ago, as well as from this decade, confirm that male infants are two to six times more likely to develop perinatal sepsis than females[12,28]. The reasons for this finding have not been elucidated. Most clinicians do not account for male gender in their assessments of newborns at risk for sepsis, although current evidence suggests that it may be prudent to do so.

Maternal Urinary Tract Infection

Unless treated and resolved before labour,

Table 1. Risk Factors of Neonatal Sepsis

Condition	Incidence of prove sepsis (%)	Incidence of prove and "highly suspected" sepsis (%)
PROM > 18-24 h[a]	1	1-2
Maternal + GBS[b]	0.5-1	1-2
PROM and + GBS[c]	4-6	6-10
+GBS and maternal fever[c]	3-5	6-10
PROM and chorioamnionitis[a]	3-8	6-10
PROM or + GBS and preterm[d]	4-6	7-11
PROM and 5-min Apgar < 6[a]	3-4	6-10
Male gender[a]	Risk > 4-fold	Risk > 4-fold

[a]Ref. 12; [b]Refs. 15-17; [c]Refs 18, 24; [d]Refs 18,12

maternal urinary tract infection is associated with an increase risk of infection in the neonates, presumably by increasing the risk of preterm birth and by increasing the rate of chorioamnionitis[29].

Additive Risks and Screening Scores

The risk factors noted earlier and in table 1 are additive. For example, St. Geme *et al*[12] observed a four to eleven fold increase in the risk of infection when either amnionitis, male gender, or prematurity were added to the primary risk factor of PROM. Furthermore, the presence of two of these risk factors raised the risk up to 25-fold, and adding all three factors raised the risk 30 fold. Using such data, St. Geme developed a screening score for infants exposed to PROM based on the three factors noted earlier, plus asphyxia and pathologic amnionitis. While the use of the scoring system to identify high risk infants decreased the frequency of "inappropriate" use of antibiotics, it did not result in a decreased total use of antibiotics in this group of babies.

The readers of this article are well aware of the nonspecific nature of the symptoms of possible neonatal sepsis, including respiratory distress, lethargy, fever or hypothermia, hypo- or hyperglycemia, hypotonia, grunting, vomiting, feeding intolerance, abdominal distension, apnea, cyanotic spells, seizures, poor perfusion or shock, petechiae or purpura, unexplained jaundice, or "not looking well"[30].

The spectrum and severity of symptoms required to evaluate for sepsis is a matter for clinical judgement and cannot be dictated by a written protocol; however, specific data for some of these symptoms are available to aid in decision making. Respiratory distress of any variety may be caused by neonatal sepsis. In the preterm infant, there is no reliable method for accurately differentiating pneumonia from respiratory distress syndrome[31-32]; in fact, the conditions may co-exist. In the term infant with mature lungs, respiratory distress is more likely to be secondary to sepsis or pneumonia. The newborn infant with meconium aspiration syndrome should also be considered infected until proven otherwise. Bacteria may have been aspirated with the meconium, or primary sepsis may have caused the fetal distress and subsequent passage and aspiration of meconium. GBS, as well as other pathogens, may cause persistent pulmonary hypertension[33], and GBS has also been associated with the development of a right-sided diaphragmatic hernia[34].

Ten percent of full-term newborns with fever ($\geq 37.8^{\circ}C$), not due to environmental causes, will have bacterial sepsis[35]. In contrast, hypothermia is a nonspecific finding during the first few days of life, as many neonates have some difficulty with temperature control during the transition to postnatal life. In one study from Saudia Arabia, however, 28% of infants with hypothermia at age $\geq$ 72 hr had bacterial sepsis or meningitis[36]. An unexplained increase in the serum bilirubin concentration, especially of the direct fraction, may be associated with sepsis, particularly urinary tract infection[37].

The decision to evaluate and treat a neonate for possible sepsis based on symptoms is a matter of clinical judgement. Certainly, almost all newborn babies with significant respiratory distress, shock, or fever should be treated pending culture results. Beyond that recommendation, the clinician must rely on careful history, physical ex-

amination, assessment of the severity of the symptoms and laboratory investigations.

DEFINITIVE, SPECIFIC DIAGNOSTIC LABORATORY TESTS

Isolation of bacteria from central body fluid is the standard and most specific method to diagnose neonatal sepsis.

Blood Culture

Sterile acquisition by venupuncture of 0.5-1.0 ml blood placed in a single, unvented culture bottle containing enriched tryptic soy broth is a standard microbiologic method available in all hospital laboratories. Acquisition of the sample from fresh umbilical artery catheter is also suitable and has a contamination rate of only 1.8%[38]. In contrast, samples from an indwelling umbilical venous catheter appear to be unreliable[39]. Special preparation of a heelstick sample may also be a satisfactory alternative, although the sensitivity of this method may be reduced compared to samples obtained by venupuncture[40]. Traditionally, the blood culture needed to be incubated for 72 hr before being considered negative, at which time 98% of positive cultures were identified[41]. This efficiency of diagnosis may vary by hospitals and by microorganisms. Recent advances in culture technique make a 48 hr reading of the culture reliable in most cases.

One of the major problems in identifying the infected neonate is that the "gold standard" (the blood culture) is tarnished. Pierce *et al*[43] and Squire *et al*[44] found that in neonates fatally sick, premortem blood cultures identified only 81-82% of infants with infection proven by immediate postmortem cultures and autopsy. It is appropriate to wonder what the false negative rate might be in the mildly symptomatic infant with negative cultures who recovers after antibiotic therapy. Furthermore, in newborn infants with clinically well-defined early-onset sepsis, there is frequently a disparity between the incidence of positive blood cultures and positive urine latex agglutination test[11]. In addition, up to 50% of neonates with congenital bacterial pneumonia as defined by clinical findings, plus a positive tracheal aspirate culture (obtained during the first 12 hr of life), had negative blood cultures[45]. Given the increase in antepartum maternal treatment with antibiotics since those studies, the blood culture may be even less sensitive today. Clearly, blood cultures are not reliable as the final arbiter for the clinical diagnosis of neonatal infection.

Lumbar puncture in the evaluation of infants for sepsis is controversial. Prior to the widespread use of intrapartum antibiotics, the blood culture could be used to identify bacteremic infants who (prior to discharge) needed to have a lumbar puncture to rule out meningitis. Approximately 30% of infants with a positive blood culture have evidence of meningitis (either a positive CSF culture or abnormal CSF values). However, blood cultures are frequently negative in infants with proven bacterial meningitis. In a recent study, Wiswell *et al* reported that 28% of 43 infants with culture proven meningitis had negative blood cultures, including four infants who were totally asymptomatic. This retrospective study focused on infants with confirmed meningitis born over a four year period at US Army hospitals. In contrast, other studies (which have collected data on infants who had a lumbar puncture as part of sepsis evaluation) have not identified asymp-

tomatic infants with meningitis, who also had a negative blood culture. In these studies very few infants with meningitis were detected even in the subset of infants with positive blood cultures. However, given the rarity of neonatal meningitis even in symptomatic infants (1/3000) the size of these studies (largest single study n = 1495) may have precluded finding significant numbers of infants with meningitis, especially in those who were asymptomatic. While Wiswell's data clearly indicates the potential for asymptomatic infants to have bacterial meningitis, it would be reassuring to have some other diagnostic test (with a high negative predictive accuracy) to let clinicians know when not to do a lumbar puncture.

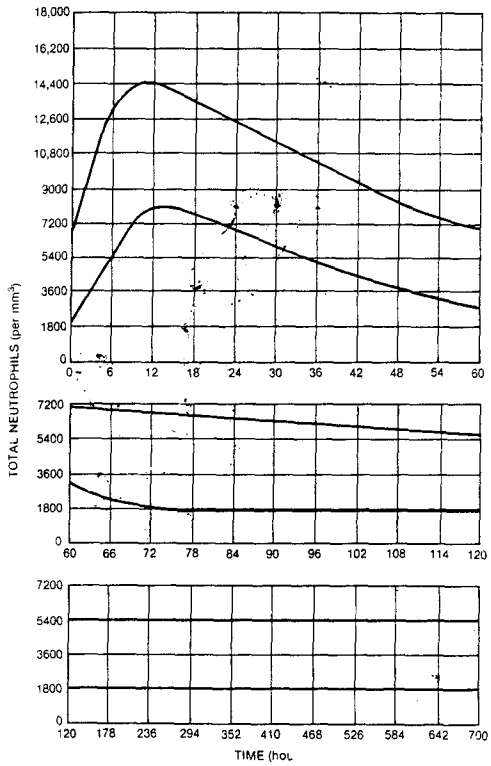

Fig. 1. Reference values for neutrophilic cells in the newborn infant.

In the absence of antepartum maternal antibiotic therapy, CSF cultures are reliable for the definitive diagnosis of bacterial neonatal meningitis; the culture usually grows within 72 hr. In contrast to the CSF culture, the preliminary examination of the CSF for cell count, differential count, glucose and protein may be difficult to interpret. CSF white blood cell counts up to 32/mm³ have been found in normal uninfected neonates. Furthermore, the mean ± 2 SD CSF cell counts have a normal upper limit of 22 cells/mm³ in preterm and 25 cells/mm³ in term neonates. However, 29% of infants with group B streptococcal meningitis may have cell counts below this range (Fig. 1)[47]. CSF glucose and protein concentrations are of little use in the definitive diagnosis of neonatal meningitis, since the normal ranges of glucose concentrations (24-119 mg/dl) and protein concentrations (20-170 mg/dl) in noninfected newborns are considerable.

Urine Culture

Urine cultures by bag specimen are notoriously unreliable and open to contamination. Therefore, it follows that they should not be obtained, except to document a proof of cure after treatment of a previously documented urinary tract infection. Although a sterile obtained sample (bladder tap) is useful in the diagnosis of nosocomial infection in the neonate[48], urine cultures are more difficult to obtain and have a low yield during the first 72 hr of life[49].

Tracheal Aspirates

Although differentiation of colonization

from infection can be difficult when assessing endotracheal tube aspirate cultures in the chronically ventilated neonate, tracheal aspirate samples are useful during the first 12 hr of life. Sherman *et al*[45] demonstrated that a positive tracheal aspirate culture may be found in 44% of infants with pneumonia and a negative blood culture. Furthermore, identification of bacteria on tracheal aspirate gram stain correlates well with clinical or pathologic pneumonia and has a 47% positive predictive accuracy for identifying bacteremic infants[50].

ADJUNCTIVE, NONSPECIFIC DIAGNOSTIC TESTS

The difficulties in accurately identifying the septic neonate have prompted evaluation of many adjunctive tests that may indicate infection, but which do not identify the inciting organism. The ideal screening tests for neonatal sepsis are those in which the probability of an abnormal test result in an infected infant is high and the probability of infection in an infant with normal test result is low. Unfortunately, no currently available laboratory tests or groups of tests provide that ideal (i.e., combined high sensitivity and high specificity). Therefore, when evaluating the utility of any laboratory test, a balance must be achieved among sensitivity, specificity, positive predictive accuracy and negative predictive accuracy based on the costs, risks and benefits of true positives, true negatives, false positive and false negative results. Since the routine treatment of neonatal sepsis (i.e., antibiotics) has little chance of causing any serious harm to the infant or psychological or economical trauma to the family (other than those associated with prolonged hospitalization) while missed cases can be catastrophic, clinicians have focused upon diagnostic tests which have a high sensitivity and negative predictive accuracy. Therefore, diagnostic tests for neonatal sepsis are most helpful when they exclude the diagnosis of sepsis in infants with a low probability of infection. It is in that population that antibiotics can either be withheld or stopped at the earliest possible time, permitting early discharge of the infant. This section will review indi-

TABLE 2. Performance of Hematologic Tests and Screens in the Diagnosis of Neonatal Sepsis

Test	Sensitivity (%)	Specificity (%)	Positive accuracy predictive (%)	Negative accuracy predictive (%)
Neutropenia (Manroe, or < 1,750/mm3)[a]	38-96	61-92	20-77	96-99
> I/T (Manroe or > 0.2)[b]	90-100	50-78	11-51	99-100
> Total immature neutrophils[c]	63-67	69-77	17-46	95
1 + 2 + 3[d]	94-100	NA	NA	100
Seven point hematologic score ≥ 3[e]	96	78	31	99
Total WBC < 5,000[f]	29	91	27	91
WBC vacuolization or toxic granulation[g]	67-81	90-93	45-59	96-98
Platelet count < 150,000[h]	22-38	82-99	20-60	93-93

vidual adjunctive tests, as well as sepsis screens, which are batteries of parameters studied in concert in order to improve diagnostic accuracy.

White Blood Cell Count

The most frequently determined adjunctive test is the white blood cell and differential cell count. For many years, the white blood cell count was felt to be of little value in the diagnosis of neonatal sepsis[57]. In the past decade, however, the work of Manroe *et al*[58] has increased the utility of this test through the establishment of normal reference ranges for total neutrophil counts and indices of immature neutrophils. The lower limit for normal total neutrophil counts in the newborn begins at 1,800/mm, rises to 7,200/mm at 12 hrs of age, and then declines and persists at 1,800/mm after 72 hrs of age. (fig. 1). A similar curve has been demonstrated for the total immature neutrophil count, which exhibits a peak count of 1,400 cells/mm at 12 hr of age. The ratio of immature to total neutrophils (I/T ratio) is ≤ 0.16 at birth, and declines to a peak value of 0.12 after 72 hr of age. Neutropenia is believed to be the best predictor of sepsis, whereas neutrophilia does not correlate well. Manroe *et al*[58] observed a 100% negative predictive value if the total neutrophil count, immature neutrophil count, and I/T were all normal. In a subsequent study, however, these indices identified only 94% of septic patients[59]. Other authors have chosen to modify these criteria based on their own hospital experience[4], or to purposefully change the sensitivity or specificity of the test based on clinical grounds[60]. The diagnostic accuracy of these indices in different studies, as well as other tests to be discussed, are presented in table 2.

The wide range of predictive values in table 2 are explained by many factors. Some studies have cluttered infants with proven sepsis with those with suspected sepsis. In addition, a considerable interobserver variability in performance of differential cell counts is likely. Study population differences may lead to variation because clinical factors other than infection may cause a hematologic change in the newborn infant. For example, maternal hypertension, perinatal asphyxia, and intraventricular hemorrhage may cause neutropenia[58]. Although maternal hypertension does not cause an elevated I/T ratio, nonspecific stresses such as asphyxia[60], maternal fever or stressful labour can elevate the I/T ratio[58,61]. White blood cell counts can be higher in capillary than in arterial or venous specimens[62,63]. Timing is also important, as the white blood cell indices in the septic infant may be normal at the time of initial evaluation, but abnormal several hours later[64,65].

The platelet count is also checked in neonates with possible sepsis. While thrombocytopenia is commonly noted in infected infants, it has a poor pensitivity (22%–38%). The specificity and negative predictive accuracy of the platelet count are both >90%.

Further efforts to improve the diagnostic accuracy of the white blood cell count have demonstrated that the presence of neutrophil vacuolization or toxic granulation is probably as good an indication of sepsis as some of the white blood cell indices[66]. Rodwell *et al*[67] developed a seven-point hematologic scoring system based on the white blood cell count, total and immature neutrophil counts and ratios, degenerative changes in neutrophils, and

thrombocytopenia. This approach appears to be useful in that a 96% sensitivity and 99% negative predictive value were obtained; however, the pitfalls of the blood count as noted above and failure to identify all septic infants, make this score a very useful but not definitive test.

C-Reactive Protein

C-reactive protein (CRP) is a rapidly responsive acute-phase reactant synthesized by the liver within 6–8 hr of an inflammatory stimulus[68]. Since infection is the most likely cause of inflammation in the neonate, elevation of CRP has been a useful marker for sepsis in many studies, although sensitivity and negative predictive values are not high enough for CRP alone to be a definitive diagnostic test (table 3)[4,6,69-71]. Like the white blood cell count, CRP may not be positive early in the course of infection[72]. Mathers and Polhandt[70] found that the diagnostic sensitivity of a CRP > 1.0 mg/dl was 16% on admission for sepsis evaluation, but 92% at 24 hr of age. Other neonatal or obstetric conditions such as meconium aspiration syndrome, asphyxia, PROM, or shock may also cause modest elevation in CRP[71].

Normal values for CRP are < 1.6 mg/dl on day 1-2 and < 1.0 mg/dl thereafter[73]. The most rapid, accurate and quantitative method for determining CRP concentration is by nephelometry. Alternatively, a positive CRP latex agglutination test on an undiluted sample corresponds to a plasma CRP concentration of 0.8 - 1.0 mg/dl. Normalization of CRP elevation appears to be a helpful tool in determining response to antimicrobial therapy and duration of treatment[72,74,75,88], and failure to mount a CRP response may be a poor prognostic sign.[72]

Gastric aspirate Gram stain and culture as shown by several studies and clinical experience is not a useful indicator of neonatal infection[83,84]. The presence of neutrophils and bacteria, however, may indicate the neonate is at risk because of exposure to chorioamnionitis[84]. In this situation, the test can be used to confirm the diagnosis of chorioamnionitis if that diagnosis is otherwise unclear.

Sepsis Screens

As is obvious from the earlier discussions, none of the adjunctive tests have sufficient sensitivity of negative predictive value in all clinical situations to exclude the diagnosis of neonatal sepsis. To improve the diagnostic capability of adjunctive tests, Philip and Hewitt[4] combined the results of five

TABLE 3. Performance of Adjunctive Tests and Screen in the Diagnosis of Neonatal Sepsis

Test	Sensitivity (%)	Specificity (%)	Positive accuracy predictive (%)	Negative accuracy predictive (%)
C-reactive[a]	47-100	83-94	6-83	71-99
WBC + CRP + I/T + mESR + heptoglobin[b]	93	88	39	99
WBC + CRP + I/T + mESR[c]	100	83	27	100

[a]Refs. 4,6,69,70,85; [b]Ref. 4; [c]Ref. 6

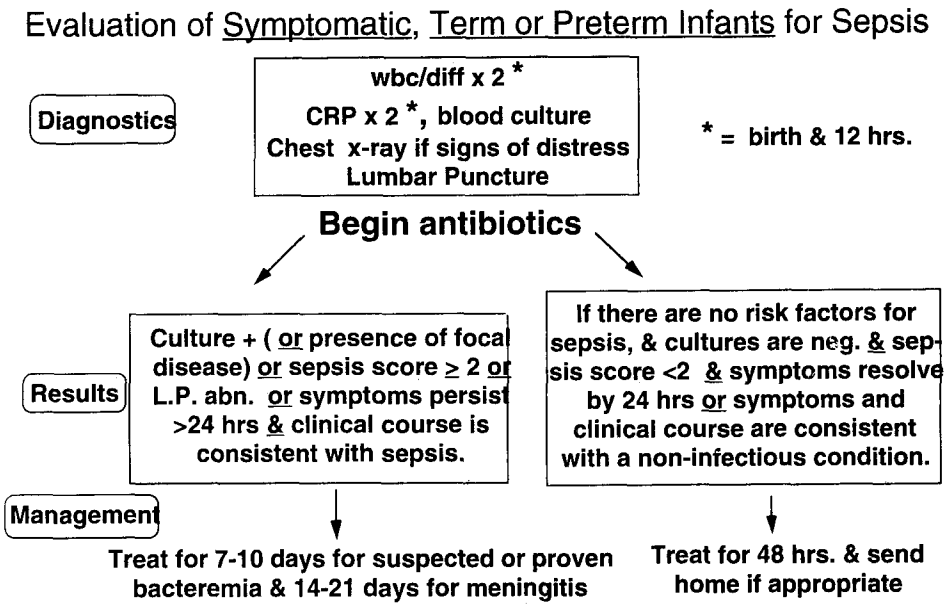

Fig. 2.

tests into a sepsis screen (white blood cell count, I/T, CRP, haptoglobin, and micro-ESR). The screen was considered positive if two or more tests were abnormal, which resulted in improved predictability for early onset sepsis (table 3); however, all patients with sepsis were still not identified, and the screen was not quite as sensitive in detecting late-onset infection[85]. Gerdes and Polin[6] performed two sepsis screens (white blood cell count, I/T, CRP, micro-ESR), 12-24 hr apart. This method identified all septic patients and had a 100% negative predictive value (table 3). One patient in that series had a normal initial screen that was positive on repeat testing. Our current sepsis screen utilize the WBC, I/T and CRP. A positive screen requires 2 points, as listed in table 4. In addition to improving his diagnostic capability, Philip demonstrated that the sepsis screen was cost-effective in decreasing antibiotic usage in his nursery[86]. Although screens combining clinical and laboratory criteria have been useful[87], many neonatologists are wary of clinical scores based on symptoms or signs and prefer to use clinical judgement as the sole judge of which symptoms are worrisome and which are ascribable to causes other than infection.

Other Diagnostic Tests

Numerous acute phase reactants and cytokines have been evaluated as diagnostic tests for neonatal sepsis, but to date, no practical tests have been developed that give better results than a combination of WBC, I/T ratio, and CRP.

DIAGNOSIS AND MANAGEMENT OF SUSPECTED SEPSIS CASES

The Symptomatic Neonate

The clinician must carefully evaluate the newborn with signs and symptoms of

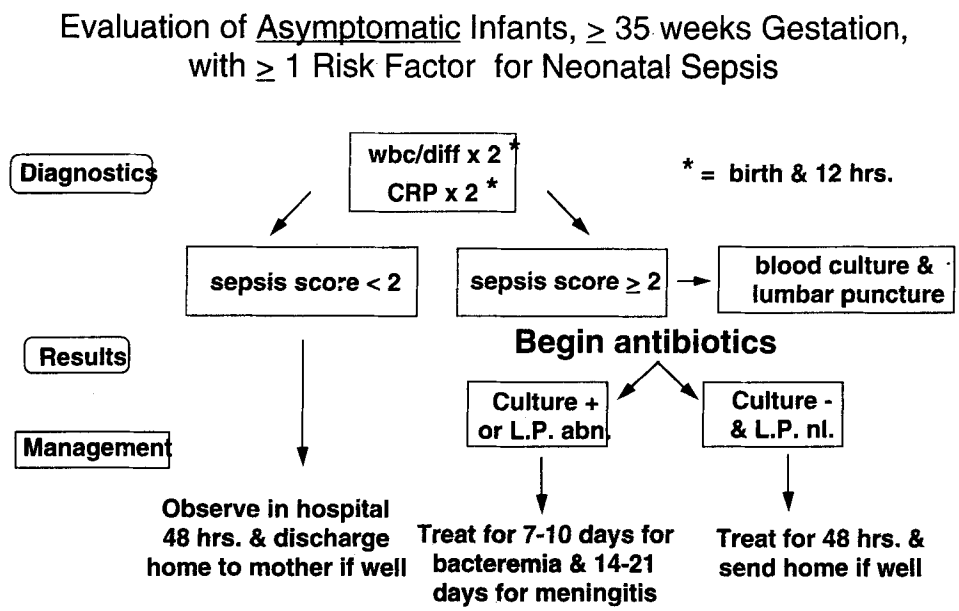
Evaluation of Asymptomatic Infants, ≥ 35 weeks Gestation,
with ≥ 1 Risk Factor for Neonatal Sepsis
Diagnostics
wbc/diff x 2 *
CRP x 2 *
* = birth & 12 hrs.
sepsis score < 2
sepsis score ≥ 2
blood culture & lumbar puncture
Begin antibiotics
Results
Culture + or L.P. abn.
Culture - & L.P. nl.
Management
Observe in hospital 48 hrs. & discharge home to mother if well
Treat for 7-10 days for bacteremia & 14-21 days for meningitis
Treat for 48 hrs. & send home if well

Fig. 3.

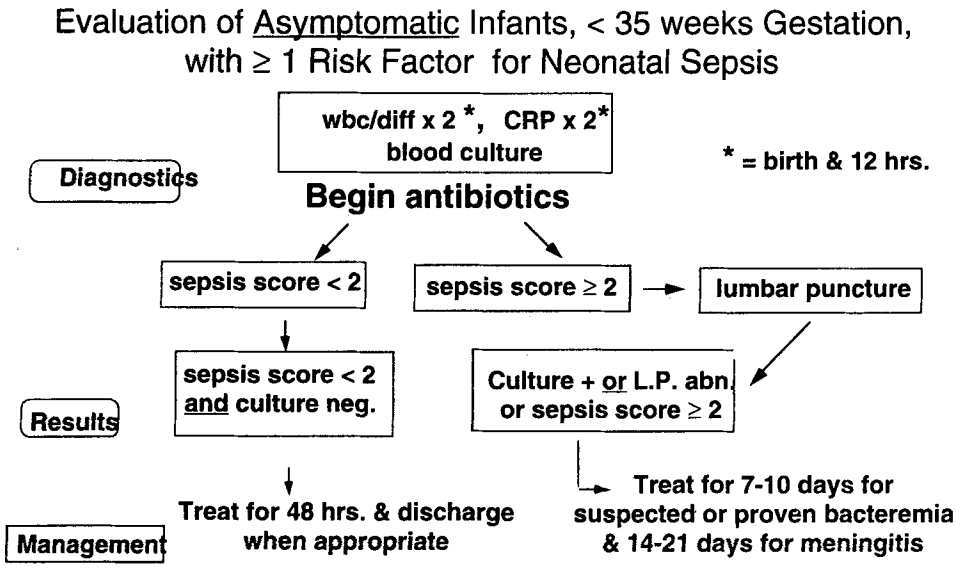
Evaluation of Asymptomatic Infants, < 35 weeks Gestation,
with ≥ 1 Risk Factor for Neonatal Sepsis
wbc/diff x 2 *, CRP x 2*
blood culture
Diagnostics
* = birth & 12 hrs.
Begin antibiotics
sepsis score < 2
sepsis score ≥ 2
lumbar puncture
sepsis score < 2 and culture neg.
Culture + or L.P. abn. or sepsis score ≥ 2
Results
Treat for 48 hrs. & discharge when appropriate
Treat for 7-10 days for suspected or proven bacteremia & 14-21 days for meningitis
Management

Fig. 4.

Appendix 2

Point Value for Laboratory Tests

Test	Point value
• Absolute neutrophil count < 1750 / mm^3	1 point
• Total white blood count < 7500 / mm^3 or > 40,000 / mm^3	1 point
• Immature / total neutrophil ratio ≥ 0.20	1 point
• Immature / total neutrophil ratio ≥ 0.40	2 points
• CRP + (≥ 1mg/dl)	1 point

Fig. 5.

possible sepsis and use clinical judgement to determine which babies need antibiotics immediately. Recommended management for the symptomatic newborn is detailed in fig. 2. The clinician must remember that the burden of proof is on him to prove there is no infection, not on the baby to prove that he or she is ill. Absence of risk factors should not dissuade one from treating a symptomatic neonate. For instance, it is well documented that ascending infection can occur in utero with intact membranes[84].

The Asymptomatic Neonate

Recommended management of the asymptomatic but at-risk term neonate is presented in fig. 3 and asymptomatic preterm in fig. 4. The decision to treat an asymptomatic at-risk neonate for possible sepsis is based on the gestational age of the neonate and the results of the sepsis screen. Because of their increased susceptibility and poor outcomes, preterm infants with risk factors should be started on antibiotics after culturing the blood. Our protocol then allows selection of which preterm infants will also have a lumbar puncture, based on the results of the sepsis screen.

Term infants with one or more risk factors may be observed with frequent vital signs and two sepsis screens done 12-24 hours apart. Asymptomatic infants with a positive sepsis screen receive blood culture, lumbar puncture, and initiation of antibiotic treatment. Duration of treatment is also defined in the protocols. Symptomatic infants are treated for a full course if their cultures, CSF exam, sepsis screen, or chest X-ray are positive. If all of these factors are negative and symptoms resolve, antibiotics may be discontinued after 48 hours. Asymptomatic infants are treated for a full course if infection is proven, but if all cultures are negative and the neonate remains well, antibiotics are discontinued after 48 hours.

CONCLUSION

Perinatally acquired bacterial neonatal sepsis is a low incidence, high risk disease with a relatively benign treatment. Accurate diagnosis is difficult because there is no definitive diagnostic test; even blood cultures have an unacceptably low sensitivity. Therefore, the clinician must accept that a number of neonates who do not have the disease will have treatment initiated for sepsis. In order to treat rapidly all infants with sepsis and to minimize therapy for those without infection, historical, clinical, and laboratory data can be used together in a management approach to achieve optimal results.

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