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Patterns of neonatal bacterial infection in the 1970's

By

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A retrospective study was carried out in a large city-county hospital nursery over the two-year period 1973—1974, to determine the incidence, mortality rate, and etiologic agents of neonatal septicemia and meningitis. One hundred of 18,465 infants admitted to the nursery service had septicemia alone and an additional 20 infants had meningitis for an incidence of 5.1 and 1.0 per 1000, respectively. In the group with septicemia the mortality rate was 38/100 (38%) and in those with meningitis 12/20 (60%). Group B streptococcus was the most frequently isolated organism, being present in 28/100 (28%) of septicemia cases and in 13/20 (65%) of those with meningeal infection. Gram positive coccal organisms comprised 47/100 (47%) of the etiologic agents of septicemia while Gram negative enteric bacilli were found in 42/100 (42%). In patients with meningitis, Gram positive cocci were present in 13/20 (65%) all being Group B streptococci; Gram negative enteric bacilli were found in 4/20 (20%). The data demonstrate the increasing incidence of Gram positive coccal organisms, primarily Group B streptococci, as the predominant cause of neonatal infection.

Septicemia with or without meningitis continues to be a significant cause of neonatal morbidity and mortality. With the advent of neonatal regional intensive care facilities, infants who may formerly have died are now evaluated and treated for prolonged periods of time in a potentially hostile bacterial environment.

A study designed to determine the incidence, mortality, and etiologic agents of septicemia/meningitis (S/M) in a large city-county hospital nursery with regional neonatal intensive care facilities was conducted over the two-year period 1973—1974.

Methods

A total of 18,465 infants were admitted to the nursery service at Jefferson Davis Hospital (JDH) in 1973—1974; 2, 111 of these were low birth weight. The hospital records of all infants with either positive blood and/or cerebrospinal fluid (CSF) cultures during the study period were reviewed and the data recorded on a standard form. Criteria for diagnosing patients as having septicemia or meningitis were strict. No patients with neural tube defects were included in the study. All blood cultures were obtained by peripheral venipuncture. Cerebrospi-

nal fluid cultures were performed by directly inoculating culture media at the time of lumbar puncture. The infections reported here represent only those occurring while the infants were in the nurseries.

Results

One hundred and twenty of these 18,465 infants had either positive blood and/or CSF cultures. One hundred had septicemia alone and 20 infants had meningitis with or without associated bacteremia. Of these 120, 105 were born at JDH and 15 were transferred from other institutions. The incidence of septicemia was 5.1 per 1000 infants (100/18,465). If the outside births were excluded the incidence was 4.6 per 1000 live births (85/18,314). Twenty infants had meningitis, one of whom was a transfer from another hospital, for an incidence of 1 per 1000 live births. Fifty of 120 infants died, 10 of whom were born at other hospitals, for an overall mortality rate of 50/100 (41.7%), and a mortality rate of 40/105 (38.1%) for those infants born at JDH. Of the group with septicemia the mortality rate was 12/20 (60%). If the outside births are excluded, then the mortality rate falls to 33.7% and 57.9%, respectively.

The culture results are shown in Table I. Group B streptococcus was the most frequently isolated organism and was found in 28/100 (28%) of the cases with septicemia and 13/20

Table I

Etiologic agents of septicemia/meningitis
1973—1974

Organism	Septicemia		Meningitis	
	Number	Percent	Number	Percent
Group B Streptococcus	28	28	13	65.0
Escherichia coli	17	17	1	5.0
Klebsiella sp.	19	19	0	—
Staphylococcus aureus	17	17	0	—
Speudomonas sp.	4	4	1	5.0
Proteus sp.	2	2	1	5.0
Enterobacter sp.	0	—	1	5.0
Haemophilus influenzae	1	1	1	5.0
Listeria monocytogenes	1	1	1	5.0
Enterococcus	2	2	0	—
Bacteroides sp.	1	1	0	—
Candida sp.	2	2	1	5.0
Mixed	6	6	0	—
Total	100		20	

(65%) of the patients with meningeal infection. Twenty-four of the streptococcal isolates were subsequently serotyped as Group B streptococci. The remaining 17 streptococcal isolates were not available for serotyping, but as their biochemical and morphologic characteristics were identical to the serotyped strains, they also were felt to be Group B streptococci. *Klebsiella sp.* and *Escherichia coli* were the most common Gram negative bacilli isolated from the blood and accounted for 19/100 (19%) and 17/100 (17%), respectively, of the cases of septicemia. However, only in one instance was *Escherichia coli* isolated from the CSF and in no instance was *Klebsiella sp.* isolated from the CSF. *Staphylococcus aureus* was the etiologic agent in 17/100 (17%) of the patients with septicemia but caused none of the cases of meningitis. All of the staphylococci were sensitive to meticillin and kanamycin, but only two of these isolates were sensitive to aqueous penicillin G. Other bacterial species found with less frequency included pseudomonas, proteus, enterobacter, *H. influenzae*, *Listeria monocytogenes*, enterococci, and *Bacteroides fragilis*. Three patients had systemic candida infection, one of whom had meningeal involvement. Six instances of septicemia represented mixed infection (Table II). Two were due to Group B streptococcus and Klebsiella, 1 to Group B streptococcus and *Escherichia coli*, 1 to Group B streptococcus and *Staphylococcus aureus*, 1 to *Escherichia coli* and enterococcus, and 1 to *Staphylococcus aureus*, and enterococcus.

Gram positive coccal organisms comprised 47/100 (47%) of the etiologic agents of septicemia while Gram negative enteric bacilli were found in 42/100 (42%). In those patients with meningitis, Gram positive cocci were present in 13/20 (65%) and all were Group B streptococci. Gram negative enteric bacilli were found in only 4/20 (20%).

Early onset infection (less than 5 days of age) occurred in 88/120 (73.3%) of the cases; 49/88 (56%) of these were due to Gram positive coccal organisms and 30/88 (34%) to Gram

Table II

Etiologic agents of mixed infections

Organism	Number
Group B Streptococcus and *Klebsiella sp.*	2
Group B Streptococcus and *Escherichia coli*	1
Group B Streptococcus and *Staphylococcus aureus*	1
Escherichia coli and enterococcus	1
Staphylococcus aureus and enterococcus	1
Total	6

negative bacilli. The remainder of the cases 9/88 (10%) represented mixed infection or other types of organisms. In those infants who became infected after 5 days of age, 20/32 (62.5%) of the causative organisms were either Gram negative enteric bacilli, of which 13/20 (65.0%) were resistant to kanamycin, or a species of candida.

Premature infants comprised 85/120 (70.8%) of the total group, and 13/20 (65%) of the infants with meningitis. No significant difference in the age of onset of disease existed between term and premature infants. Forty-two out of fifty (84%) of the deaths occurred in the early onset group, and 30 of these 42 deaths occurred within 48 hours of birth.

Twenty-seven per cent of the mothers had received no prenatal care prior to delivery and 74.2% of the mothers had some form of obstetric complication either during pregnancy or during labor and delivery. Prolonged rupture of the fetal membranes greater than 24 hours occurred in 21/120 (17.5%) of the patients.

There was a male to female ratio of 1.7 : 1 (63 males and 37 females) in the group with septicemia and a ratio of 1.5 : 1 (12 males and 8 females) in the meningitis group.

Discussion

The incidence of neonatal septicemia has been reported from 1/500 to 1/600 live births [9, 12, 13], and neonatal meningitis has been found in approximately 0.4/1000 live births [11, 15].

It is difficult to explain why the incidence of S/M should be so much higher than that found in previous studies. Several factors may account for this apparent discrepancy. The population served by JDH has a large percentage of high risk deliveries. Fully 25% of the mothers who deliver at JDH have no prenatal care and all belong to a low socio-economic group. As previously noted, maternal complications were frequent in the study group and there was a high incidence of prematurity. Both factors have been related to increased risk of neonatal infection [13, 16, 19]. Because of the improved life support systems now available, many premature infants are exposed to resistant bacterial flora within the hospital for prolonged periods of time thus increasing their risk of becoming infected. It is nursery policy to obtain blood, urine and cerebrospinal fluid cultures on any infant who is judged to be at risk and whose clinical course suggests infection, regardless of any other disease entity felt to be primarily responsible for the infant's condition. This policy would be expected to increase the number of infants identified as infected.

The increased role of the Group B streptococcus in neonatal infection is probably related to the increased incidence of maternal and neonatal colonization. Baker et al. found that 25% of all mothers and infants in our hospital had Group B streptococcal colonization at the time of deliv-

ery [1]. Similar rates of colonization also have been noted in studies involving middle-class college students in the northeastern portion of the country [3]. Why this high colonization rate exists is not known at present.

The increase in the incidence of septicemia due to *Staphylococcus aureus* is unexplained. Most of these infants were symptomatic early in life and represented early onset infection (14/17). No increase in staphylococcal colonization was noted during the study period nor were bathing or cord care policies altered (Unpublished data).

Late onset infection is often equated with nosocomial infection. Several authors have related acquisition of resistant organisms to prior antibiotic treatment and prolonged hospitalization [2, 6, 8]. Our data support this in that resistant Gram negative bacilli were frequently found in those infants with late onset disease.

Prior to the mid 1940's beta-hemolytic streptococci were the predominant organisms isolated from infected neonates [7, 14]. Beginning in the late 1940's and progressing through the mid 1960's an increasing proportion of neonatal infections were due to Gram negative enteric bacilli [5, 9—11, 14—16]. In the late 1960's and early 1970's this pattern has again changed with Gram positive coccal forms, particularly Group B streptococcus, becoming increasingly prevalent [1, 17, 18]. A further shift is demonstrated by our data with over 47% of the patients with septicemia and 65% of those with meningitis having Gram positive coccal organisms isolated, primarily Group B streptococci, and only 42% and 20%, respectively, having infections due to Gram negative coliform organism.

Thus a periodicity or "wave form" effect becomes apparent regarding the various bacterial pathogens implicated in neonatal infection (Figs 1, 2). Although the reasons underlying this phenomenon are unclear, recent work by Baker and Kasper may offer a

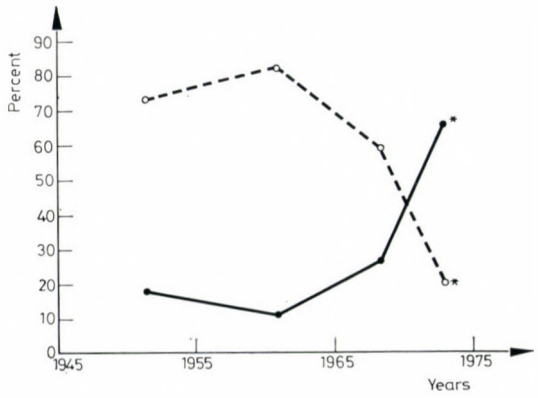

FIG. 1. Incidence of Gram positive coccal (—) vs Gram negative enteric bacilli (- - -) in neonatal septicemia [7, 9, 10, 14, 17]. *Jefferson Davis Hospital

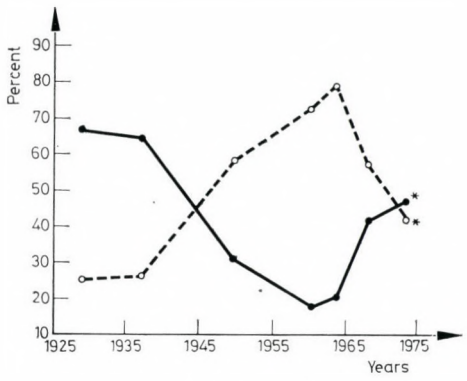

FIG. 2. Incidence of Gram positive coccal (—) vs Gram negative enteric bacilli (- - -) in neonatal meningitis [5, 16, 17]. *Jefferson Davis Hospital

possible explanation [4]. Their data suggest that transplacental transfer of maternal antibody protects infants from invasive Group B streptococcal infection with Type III strains. If maternal colonization and subsequent neonatal infection by pathogenic bacteria can be related to the maternal immune experience and subsequent production of protective levels of transplacental IgG antibody, then a mechanism explaining the observed periodicity can be hypothesized. As maternal antibody levels rise or fall in response to colonization by individual bacteria then the incidence of neonatal infection would be expected to change in a cyclic manner.

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