

Chapter 6: The young infant under 2 months of age

Section A: Etiology

Introduction

The etiology of pneumonia, sepsis, and meningitis in infants under the age of 2 months in developing countries remains only partially defined. While results of studies from developing countries throughout the world have been published, several factors make their interpretation and comparison difficult. Most of the studies are from university hospitals and include a large proportion of premature and other high risk infants, as well as infants transferred from other health facilities. Thus, they may not accurately reflect the distribution of organisms causing neonatal sepsis in the general population. Some studies do not report bacteriological methods, and those that do seldom include sufficient detail to assess their ability to isolate fastidious organisms. The organisms defined as "contaminants" in various studies differ, with some studies including organisms such as *Staphylococcus epidermidis* (which is an unlikely pathogen, except in very small premature infants and/or infants with invasive procedures) as common etiological agents. Similarly, in many reports it is difficult to judge whether standardized methods for antimicrobial susceptibility testing have been used, if a control organism has been included in every test, and what zone size was used to distinguish "susceptible" from "resistant". In addition, since the etiological agents causing disease in the first several days of life differ from those causing infection later in the neonatal period, results should be reported separately for early and late neonatal infections; this is done in some studies and not in others. Finally, the selection by clinical suspicion of infants for investigation, and the lack of comparison to non-septic or culture-negative infants, make evaluation of the sensitivity and specificity of reported clinical signs difficult.

Despite these drawbacks, several patterns emerge (see accompanying tables). Gram negative organisms, primarily *E. coli* and *Klebsiella*, account for the majority of infections in most studies. The proportions of other gram negative isolates, including *Pseudomonas*, *Acinetobacter*, and *Proteus* differ markedly between studies, and may reflect the presence of contaminants, or nosocomial infection among high risk infants in an intensive care setting. *S. aureus* was the most commonly isolated gram positive organism. Group B streptococcus, an important pathogen in many developed countries, has been isolated commonly only in Jamaica and in recent studies from Saudi Arabia and Pakistan. The relative absence of Group B streptococci, as well as *S. pneumoniae* and *H. influenzae* (which are major causes of infection in older infants) may reflect the fact that they rarely cause neonatal disease in developing countries or that the laboratory methods used were unable to isolate these fastidious organisms.

The role of organisms requiring special isolation techniques, such as *Chlamydia*, *Ureaplasma*, *Mycoplasma*, *Pneumocystis*, and viruses in the etiology and sequelae of serious illness, including pneumonia, early in life has not been studied extensively in developing countries. Two reports, one on the etiology of perinatal events and the other on agents causing pneumonia up to 3 months of age, provide clues to the importance of these agents. However, for the moment the role of these agents, particularly *Ureaplasma* and *Pneumocystis*, remains controversial.

This section contains summary tables of the etiological agents of neonatal septicaemia reported from developing countries. It also contains annotations of some of these reports, a perinatal study from Ethiopia, and longitudinal studies of neonatal septicaemia and etiological agents of pneumonia from the United States. No attempt has been made to annotate or summarize

the extensive literature on neonatal septicaemia from developed countries. Also, it is recognized that the organisms causing septicaemia in the first part of the first month of life are not necessarily the same as those causing pneumonia, sepsis and meningitis among infants 2-8 weeks of age. Very limited data from developing countries are available on etiology in the latter age group.

Summary table of reports of neonatal septicaemia in developing countries

First author	Place	Study size	Infants in-born	Early infections	Culture methods described	Most prevalent organisms	Sensitivity to gentamicin (%)	Infection per 1000 live births	Mortality (%)
Myrgard 1971	Addis Ababa, Ethiopia	18	-	100% <24h	yes	<i>S. viridans</i> <i>Enterococcus</i> spp. <i>Klebsiella</i> - <i>Aerobacter</i> <i>S. epidermidis</i>	-	-	50
Choudhury 1975	New Delhi, India	49	100%	-	no	<i>Klebsiella</i> spp. <i>E. coli</i> <i>S. aureus</i>	96 100 100	34	65
Tafari 1976	Addis Ababa, Ethiopia	107	-	40% <24h	yes	<i>S. epidermidis</i> <i>E. coli</i> <i>Klebsiella</i> spp.	100 98	4	38
Alausa 1977	Ibadan, Nigeria	46	-	-	yes	<i>S. aureus</i> <i>Klebsiella</i> spp. <i>P. aeruginosa</i>	-	-	41
Guha 1978	New Delhi, India	160	100%	-	no	<i>E. coli</i> <i>Klebsiella</i> <i>Staphylococci</i>	94 93 89	27	24
Singh 1978	New Delhi, India	105	-	-	no	<i>P. aeruginosa</i> <i>S. albus</i> <i>S. aureus</i> <i>K. pneumoniae</i>	-	19	55
Omene 1979	Benin City, Nigeria	74	57%	72% <7days	no	<i>E. coli</i> <i>S. aureus</i> <i>K. aeruginosa</i>	-	6	42

Summary table of reports of neonatal septicaemia in developing countries

First author	Place	Study size	Infants in-born	Early infections	Culture methods described	Most prevalent organisms	Sensitivity to gentamicin (%)	Infection per 1000 live births	Mortality (%)
Bhakoo 1980	Chandigarh, India	307	60%	80% <7days	yes	S. aureus E. coli K. aeruginosa	97 100 86	—	64
Dawodu 1980	Ibadan, Nigeria	88	80%	69% <48h	yes	Klebsiella S. aureus E. coli	100 98	9	35
Saxena 1980	New Delhi, India	49	0%	—	no	Micrococci Myma polymorpha Coagulase positive Staphylococci	—	—	52
Tafari 1980	Addis Ababa, Ethiopia	344	—	76% <72h	no	E. coli S. epidermidis Klebsiella spp.	—	6	41
Ohlsson 1981	Riyadh, Saudi Arabia	29	17%	45% <7days	no	Salmonella spp. K. pneumoniae E. coli	—	—	45
El Rifai 1982	Riyadh, Saudi Arabia	54	0%	—	no	S. aureus E. coli Klebsiella	—	—	—
Yardi 1984	Bombay, India	127	—	—	yes	Klebsiella spp. Coagulase positive Staphylococci Pseudomonas spp.	—	—	67

Summary table of reports of neonatal septicaemia in developing countries

First author	Place	Study size	Infants in - born	Early infections	Culture methods described	Most prevalent organisms	Sensitivity to gentamicin (%)	Infection per 1000 live births	Mortality (%)
Okolo 1985	Benin City, Nigeria	177	50%	41% <48h	yes	S. aureus Klebsiella spp. Pseudomonas spp.	85	6	31
Khatua 1986	Calcutta, India	55	-	71% <5days	yes	K. pneumoniae E. coli Citrobacter freundii	100 100 100	7	69
Monga 1986	Bombay, India	264	-	-	no	Klebsiella S. aureus P. aeruginosa	73 79 49	-	-
Ohlsson 1986	Riyadh, Saudi Arabia	49	16%	39% <48h	no	Klebsiella, Serratia E. coli S. aureus	-	2	33
Sinha 1986	Calcutta, India	55	0%	-	no	P. aeruginosa Klebsiella spp. E. coli	-	-	62
Akhtar 1987	Peshawar, Pakistan	174	-	65% <7days	yes	Group B streptococci S. aureus P. aeruginosa	63	-	-
MacFarlane 1987	Kingston, Jamaica	71	-	-	yes	Group B streptococci K. pneumoniae S. aureus	-	1	36

Summary table of reports of neonatal septicaemia in developing countries

First author	Place	Study size	Infants in-born	Early infections	Culture methods described	Most prevalent organisms	Sensitivity to gentamicin (%)	Infection per 1000 live births	Mortality (%)
Namdeo 1987	Rewa, India	24	-	46% <7days	yes	E. coli P. pyocyaneous K. aeruginosa	-	-	46
Sharma 1987	New Delhi, India	1559	-	-	no	E. coli Klebsiella spp. Staphylococci	28 27 29	-	45
Chugh 1988	New Delhi, India	45	38%	69% <7days	no	Klebsiella spp. S. aureus P. aeruginosa	91	-	53
Owa 1988	Ilesha, Nigeria	30	-	44% <72h	yes	S. aureus atypical coliforms E. coli	100	17	-
Abu-Osba 1989	Eastern Province, Saudi Arabia	75	-	53% <72h	no	S. epidermidis E. coli Klebsiella, Enterobacter spp.	-	2	-
Haque 1990	Riyadh, Saudi Arabia	190	-	74% <48h	yes	S. epidermidis S. aureus Klebsiella spp.	-	12	13

		Kleb	E.coli	Staph coag +	Staph coag -	Staph undiff	Peaud	Acin	Prot	Salm	GBS	Faec	GDS	Pneum	Haem	Other	Total isolates
a) Saudi Arabia																	
Riyadh	1980	8	4	3	0	0	2	0	0	9	0	0	0	0	0	3	29
Riyadh	1981	9	12	14	6	0	2	0	0	7	0	0	0	0	0	2	54
Riyadh	1984	11	9	4	3	0	2	0	0	2	3	0	0	2	1	16	53
Riyadh	1988	18	10	33	68	0	9	0	0	0	6	0	0	0	0	46	190
Eastern	1986	12	12	0	14	0	0	0	0	0	9	0	11	0	0	17	75
Subtotal		58	47	54	91	0	15	0	0	18	18	0	11	2	3	84	401
		14%	12%	13%	23%	0%	4%	0%	0%	4%	4%	0%	3%	0%	1%	21%	100%
b) Nigeria																	
Ibadan	1976	14	5	15	0	0	6	0	2	0	0	0	0	0	0	4	46
Ibadan	1978	24	18	22	6	0	4	1	1	1	0	5	0	0	0	6	88
Benin	1977	8	25	18	3	0	5	0	0	0	0	0	0	0	0	15	74
Benin	1983	38	21	50	23	0	34	3	8	4	0	1	0	5	0	37	224
Ilesha	1986	4	4	8	1	0	2	0	0	0	0	2	0	0	1	9	31
Subtotal		88	73	113	33	0	51	4	11	5	0	8	0	5	1	71	463
		19%	16%	24%	7%	0%	11%	1%	2%	1%	0%	2%	0%	1%	0%	15%	100%
c) Ethiopia																	
Addis Ababa	1971	2	1	1	2	0	0	0	1	0	0	0	0	0	0	11	18
Addis Ababa	1976	14	19	28	3	0	2	7	3	2	0	0	1	0	0	28	107
Addis Ababa	1980	39	65	21	65	0	10	27	16	0	10	0	17	0	0	74	344
Subtotal		55	85	50	70	0	12	34	20	2	10	0	18	0	0	113	469
		12%	18%	11%	15%	0%	3%	7%	4%	0%	2%	0%	4%	0%	0%	24%	100%
d) Jamaica																	
Kingston	1985	16	5	9	0	0	0	0	0	0	25	0	6	0	0	11	72
Macfarlane		22%	7%	13%	0%	0%	0%	0%	0%	0%	35%	0%	8%	0%	0%	15%	100%
e) India																	
Bombay	1982	100	13	20	0	0	15	0	0	0	0	0	0	0	0	13	161
Bombay	1983	50	8	23	7	0	19	0	4	7	0	0	0	0	0	9	127
Bombay	1984	29	16	32	0	0	20	0	0	0	0	0	0	0	0	6	103
Subtotal		179	37	75	7	0	54	0	4	7	0	0	0	0	0	28	391
		46%	9%	19%	2%	0%	14%	0%	1%	2%	0%	0%	0%	0%	0%	7%	100%
Calcutta	1979	13	16	11	0	0	24	0	0	0	0	2	0	0	0	0	55
Calcutta	1983	14	10	5	2	0	7	0	3	0	3	0	0	0	0	11	55
Subtotal		27	26	16	2	0	31	0	3	0	3	2	0	0	0	11	110
		22%	21%	13%	2%	0%	26%	0%	2%	0%	2%	2%	0%	0%	0%	9%	100%

Distribution of organisms in reports of neonatal septicaemia by country and date of study
(final year of data collection)

	Kleb	E. coli	Staph coag +	Staph coag -	Staph undiff	Pseud	Acin	Prot	Salm	GBS	Faec	GDS	Pneum	Haem	Other	Total isolates
Chandig	11	23	17	0	0	17	0	0	0	0	7	0	0	0	57	132
Chandig	9	25	40	0	0	11	0	0	0	0	10	0	0	0	18	113
Chandig	21	14	34	0	0	4	0	0	0	0	14	0	0	0	26	113
Subtotal	41	62	91	0	0	32	0	0	0	0	31	0	0	0	101	358
	11%	17%	25%	0%	0%	9%	0%	0%	0%	0%	9%	0%	0%	0%	28%	100%
N Delhi	17	14	14	3	0	8	0	0	0	0	2	0	0	0	3	61
N Delhi	42	64	0	36	0	10	0	0	0	0	0	0	2	0	6	160
N Delhi	14	13	19	22	0	24	0	2	0	0	0	0	0	0	11	105
N Delhi	13	5	14	0	0	7	0	0	0	0	0	0	0	0	22	61
N Delhi	213	169	0	59	0	28	64	14	4	0	0	0	0	0	75	627
N Delhi	197	193	0	22	8	8	30	5	6	0	0	0	0	0	22	483
N Delhi	50	64	0	13	4	11	11	7	8	0	0	0	0	0	4	161
N Delhi	49	109	0	34	10	10	22	13	19	0	0	0	0	0	32	288
N Delhi	31	2	5	1	0	4	0	0	0	0	0	0	0	0	2	45
Subtotal	626	633	52	164	164	104	127	41	37	0	2	0	2	0	177	1991
	31%	32%	3%	1%	8%	5%	6%	2%	2%	0%	0%	0%	0%	0%	9%	100%
Rewa	5	7	5	0	0	6	0	1	0	0	0	0	0	0	0	24
Namdeo	21%	29%	21%	0%	0%	25%	0%	4%	0%	0%	0%	0%	0%	0%	0%	100%
Subtotal	878	765	239	35	164	227	127	49	44	3	35	0	2	0	317	2885
(India)	30%	27%	8%	1%	6%	8%	4%	2%	2%	0%	1%	0%	0%	0%	11%	100%
f) Pakistan	9	94	16	0	0	10	0	6	0	32	0	0	3	0	4	174
Peshawar	5%	54%	9%	0%	0%	6%	0%	3%	0%	18%	0%	0%	2%	0%	2%	100%
Overall total	1104	1069	481	229	164	315	165	86	69	88	43	35	12	4	600	4453
	25%	24%	11%	5%	4%	7%	4%	2%	2%	2%	1%	1%	0%	0%	13%	100%

Kleb = Klebsiella, Enterobacter
 E. coli = E. coli
 Staph coag+ = Staphylococcus, coagulase positive
 Staph coag- = Staphylococcus, coagulase negative
 Staph undiff = Staphylococcus, not stated whether coagulase positive or negative
 Pseud = Pseudomonas
 Acin = Acinetobacter
 Prot = Proteus
 Salm = Salmonella
 GBS = Group B Streptococcus
 Faec = S. faecalis
 GDS = Group D Streptococcus
 Pneum = S. pneumoniae
 Haem = H. influenzae

References for the tables on neonatal septicaemia in developing countries

* Indicates report annotated in this section

Myrgard H. Septicaemia in newborns. *Ethiop Med J*, 1971; 9: 181-186.

Choudry P, Srivastava G, Aggarwal DS, Saini L, Gupta S. Bacteriological study of neonatal infection. *Indian Pediatr*, 1975; 12(6): 459-463.

Tafari N, Ferede A, Girmani M, Mullen S, Tsige-Roman A. Neonatal septicaemia. *Ethiop Med J*, 1976; 14: 169-177.

Alausa KO, Montefiore D, Sogbetun AO, Ashiru JO, Onile BA, Sobayo E. Septicaemia in the tropics: a prospective epidemiological study of 146 patients with a high case fatality rate. *Scand J Infect Dis*, 1977; 9: 181-185.

Guha DJ, Jaspal D, Das K, Guha AR, Khatri RL, Srikumar R. Outcome of neonatal septicaemia: a clinical and bacteriological profile. *Indian Pediatrics*, 1978; 15(5): 423-427.

Singh M. Nosocomial bacterial infections among newborn babies. *Indian J Pediatr*, 1978; 45(369): 314-317.

* Omene JA. Neonatal septicaemia in Benin City, Nigeria: a review of 74 cases. *Trop Geogr Med*, 1979; 31: 35-39.

* Bhakoo ON. Neonatal bacterial infections at Chandigarh: a decade of experience. *Indian J Pediatr*, 1980; 47(388): 419-424.

* Dawodu AH, Alausa OK. Neonatal septicaemia in the tropics. *Afr J Med Sci*, 1980; 9: 1-6.

Saxena S, Anand NK, Saini L, Mittal SK. Bacterial infections among home delivered neonates: clinical picture and bacteriological profile. *Indian Pediatrics*, 1980; 17(1): 17-24.

Tafari N, Ljungh-Wadstrom A. Consequences of amniotic fluid infection: early neonatal septicaemia. *Excerpta Medica*, 1980; 47(388): 419-424.

* Ohlsson A, Serenius F. Neonatal Septicaemia in Riyadh, Saudi Arabia. *Acta Paediatr Scand*, 1981; 70: 825-829.

El Rifai MR. A study of 214 neonates with infection in the Maternity and Children's Hospital of Riyadh, Saudi Arabia. *Ann Trop Pediatr*, 1982; 2: 119-122.

Yardi D, Gaikwad S, Deodhar L. Incidence, mortality, and bacteriological profile of septicaemia in pediatric patients. *Indian J Pediatr*, 1984; 51(409): 173-176.

* Okolo AA, Omene JA. Changing patterns of neonatal septicaemia in an African city. *Ann Trop Paediatr*, 1985 Sep; 5(3): 123-126.

- * Khatua SP, Das AK, Chatterjee BD, Khatua S, Ghose B, Saha A. Neonatal septicaemia. *Indian J Pediatr*, 1986; 53(4): 509-514.

- Monga K, Fernandez A, Deodhar L. Changing bacteriological patterns in neonatal septicaemia. *Indian J Pediatr*, 1986; 53(4): 505-508.

- * Ohlsson A, Bailey T, Takieddine F. Changing etiology and outcome of neonatal septicaemia in Riyadh, Saudi Arabia. *Acta Paediatr Scand*, 1986; 75: 540-544.

- Sinha N, Deb A, Mukherjee AK. Septicaemia in neonates and early infancy. *Trop Pediatr*, 1987; 33: 302-304.

- * Akhtar T, Zai S, Khatoon J, Zohra A, Taj Roghani M, Ahmad A. A study of Group B streptococcal colonization and infection in newborns in Pakistan. *J Trop Pediatr*, 1987; 33: 302-304.

- McFarlane DE. Neonatal Group B streptococcal septicaemia in a developing country. *Acta Paediatr Scand*, 1987; 76: 470-473.

- Namdeo UK, Singh HP, Rajput VJ, Shrivastava KK, Namdeo S. Bacteriological profile of neonatal septicaemia. *Indian Pediatr*, 1987; 24: 53-56.

- Sharma PP, Halder D, Dutta AK, Dutta R, Bhatnagar S, Bali A, Kumari S. Bacteriological profile of neonatal septicaemia. *Indian Pediatr*, 1987; 24: 1011-1017.

- Chugh K, Aggarwal BB, Kaul VK, Arya SC. Bacteriological profile of neonatal septicaemia. *Indian J Pediatr*, 1988; 55(6): 961-965.

- Owa JA, Olusanya O. Neonatal bacteraemia in Wesley Guild Hospital, Ilesha, Nigeria. *Ann Trop Paediatr*, 1988; 8: 80-84.

- Abu-Osba YK, Mallouh AA, Hann RW. Incidence and causes of sepsis in glucose-6-phosphate dehydrogenase-deficient newborn infants. *J Pediatr*, 1989; 114(5): 748-752.

- Haque KN, Chagia AH, Shaheed MM. Half a decade of neonatal sepsis, Riyadh, Saudi Arabia. *J Trop Pediatr*, 1990; 36: 20-23.

Bhakoo ON, Agarwal KC, Narang A, Bhattacharjee S.

Prognosis and treatment of neonatal septicemia: a clinico-bacteriological study of 100 cases.
Indian Pediatr, 1974; 11(8): 519-528.

In order to investigate the causative organisms, their pattern of antimicrobial sensitivity, and other factors determining the outcome of neonatal septicaemia, a review was made of 100 episodes of neonatal septicaemia occurring over a three-year period at the Postgraduate Institute of Medical Education and Research, Chandigarh, India.

Septicaemia was diagnosed when a single positive blood culture was found in a neonate with clinical signs and response to treatment supporting the diagnosis. The methods used for bacterial culture and for antimicrobial sensitivity testing were fully described. The methods used would make isolation of *Haemophilus* unlikely. The overall mortality rate was 64%; low-birth-weight and premature infants experienced higher mortality. Pneumonia was the most common associated condition, occurring in 26 neonates. The organisms recovered from blood culture and their antimicrobial sensitivities included:

			Gentamicin	Penicillin	Cephaloridine
<i>E. coli</i>	23	(23%)	90%		66%
<i>S. aureus</i>	17	(17%)	100%	25%	83%
<i>P. aeruginosa</i>	17	(17%)	94%		
<i>A. faecalis</i>	11	(11%)	50%	0%	17%
<i>Klebsiella</i> spp.	14	(14%)			
<i>Enterobacter</i>	11	(11%)	86%	0%	29%
<i>S. faecalis</i>	7	(7%)	100%	0%	20%
Total isolates	100				

Abdominal distension, respiratory distress, apneic spells, sclerema, and absence of fever were found more often in neonates who expired than those that recovered, but only the final two factors reached statistical significance. The authors concluded that continuing evaluation of the bacteriology and sensitivity patterns in neonatal septicaemia was desirable so as to modify therapeutic strategies.

Dawodu AH, Alausa OK.
Neonatal septicaemia in the tropics.
Afr J Med Sci, 1980; 9: 1-6.

The purpose of the study was to document the clinical pattern of neonatal septicaemia, including the causative organisms and their antibiotic sensitivities, at the University College Hospital, Ibadan, Nigeria.

The medical records of infants, aged from birth to 30 days, with the diagnosis of septicaemia, were reviewed for a two-and-a-half-year period. Septicaemia was diagnosed when a positive blood culture was found in a patient with perinatal history or clinical features suggestive of septicaemia. The methods used for bacterial culture were fully described, but the methods used for antimicrobial sensitivity testing were not described. The methods used would make isolation of *Haemophilus* unlikely. Septicaemia was considered early onset if the diagnosis was made within the first 48 hours of life, and late onset if made between 48 hours and 30 days of age.

During the study period, 70 of 7626 hospital live births were diagnosed as neonatal septicaemia (9 per 1000 live births). An additional 18 septic neonates were referred from other hospitals, maternity units, or home. Among the affected neonates, the male to female ratio was 1.9:1, and preterm infants significantly outnumbered term infants. The overall mortality rate was 35%. Among 61 infants with early onset sepsis, the mortality was 36%, while it was 26% among 23 infants with late onset sepsis. Jaundice, lethargy, respiratory distress, and fever were the most common clinical signs in the cases, but no comparison was made with a control group or with suspected neonates with negative cultures.

The distribution of etiological agents, isolated from blood cultures, and their antimicrobial sensitivities were:

			Gentamicin	Penicillin	Cephaloridine
<i>Klebsiella</i> spp.	24	(27%)	100%	25%	
<i>S. aureus</i>	22	(25%)			95%
<i>E. coli</i>	18	(20%)	98%	25%	
<i>S. epidermidis</i>	6	(7%)			
<i>S. faecalis</i>	5	(6%)			
Total isolates	88				

Klebsiella spp. were found significantly more often in early onset than in late onset sepsis. The authors discussed the high rate of sepsis found in this study, and related it to the large number of high risk pregnancies and babies. They concluded that, in their setting, gentamicin in combination with cloxacillin or methicillin (because of the high prevalence of *S. aureus*) should be used as initial therapy in cases of suspected neonatal septicaemia.

Freedman RH, Ingram DL, Gross I, Ehrenkranz A, Warshaw JB, Baltimore RS.
A half century of neonatal sepsis at Yale: 1928 to 1978.
Am J Dis Child, 1981; 135: 140-144.

The purpose of the report was to describe the experience in neonatal septicaemia at the Yale-New Haven Hospital, New Haven, Connecticut, USA, over the 13-year period ending in 1978, and to compare it with earlier reports from the same hospital covering the periods 1928 to 1933, 1933 to 1957, and 1958 to 1965.

The bacteriology records of cultures obtained from infants admitted to the Newborn Special Care Unit, over a 13-year period, were reviewed. The methods used for bacterial culture were not described. Among infants born at the Yale-New Haven Hospital, the incidence for early onset sepsis (under 48 hours of age) varied from approximately 1 per 1000 to 3.89 per 1000 live births, and late onset sepsis (from 48 hours to 30 days of age) ranged from 0.85 to 2.54 per 1000 live births. There were 384 isolates recovered from 359 infants, 120 referred from elsewhere and 239 born in the hospital. The male to female ratio among all study infants was 1.46:1 and the overall mortality was 26%. The bacterial isolates from blood culture included:

<i>E. coli</i>	122	(32%)
Group B <i>Streptococcus</i>	97	(25%)
<i>Klebsiella</i> , <i>Enterobacter</i>	56	(15%)
<i>S. aureus</i>	20	(5%)
Group D <i>Enterococcus</i>	13	(3%)
<i>Haemophilus</i> spp.	11	(3%)
Total isolates	384	

Among commonly found pathogens, Group B *Streptococcus* and *Haemophilus* were frequently found with early onset sepsis, while the majority of *S. aureus* and *Klebsiella* isolates were noted after 48 hours of life. A review of earlier findings at the hospital documented Group A beta-haemolytic *Streptococcus* as the predominant agent in the 1930s and early 1940s, replaced by "coliform" organisms in the late 1940s and early 1950s. Very few Group B *Streptococci* were identified prior to 1966, but by the late 1960s it had surpassed *E. coli* as the most commonly isolated pathogen in neonatal sepsis, then declined in both incidence and mortality. Case mortality declined continuously from approximately 85% in 1935 to 29% in the current series.

Khatua SP, Das AK, Chatterjee BD, Khatua S, Ghose B, Saha A.

Neonatal septicaemia.

Indian J Pediatr, 1986; 53(4): 509-514.

This study was conducted in order to investigate the incidence of neonatal septicaemia, its presenting features, bacteriology and antimicrobial sensitivity, and outcome at the Calcutta Medical College, Calcutta, India.

Among 8386 hospital live births, 92 consecutive episodes of clinical neonatal septicaemia were observed over a one-year period. Blood cultures were positive in 55 (60%), a rate of 6.6 per 1000 live births. The methods used for bacterial culture, aerobic and anaerobic, were fully described, but the methods used for antimicrobial sensitivity testing were not described. The mortality among culture-positive cases was 69%. The organisms isolated and their sensitivity to antimicrobials were:

		Gentamicin	Penicillin	Cephaloridine
<i>K. pneumoniae</i>	12 (22%)	100%	25%	0%
<i>E. coli</i>	10 (18%)	100%	20%	0%
<i>Citrobacter freundii</i>	8 (15%)	100%	0%	0%
<i>P. aeruginosa</i>	7 (13%)	100%	40%	0%
<i>S. aureus</i>	5 (9%)			
Total isolates	55			

Refusal to feed, lethargy, diarrhoea, hypothermia, abdominal distention, jaundice, and vomiting were the most common presenting features. Respiratory distress, apnoeic spells, convulsions, and sclerema were late features and were associated with poor prognosis. Clinical signs were not compared with those found in a control group or with suspected but culture-negative infants. A higher rate of sepsis and higher mortality were found in males, premature infants, and those with low birth weight.

Naeye RL, Tafari N, Judge D, Gilmour D, Marboe C.
Amniotic fluid infections in an African city.
J Pediatr, 1977; 90(6): 965-970.

To test the hypothesis that congenital pneumonia, originating in an amniotic fluid bacterial infection, has a role in the excessive perinatal mortality characteristic of many developing countries, the authors conducted a study of perinatal mortality in the hospitals and clinics affiliated with the Addis Ababa University Faculty of Medicine, Addis Ababa, Ethiopia.

Over a two-year period, 703 pregnancies producing stillbirths and 316 resulting in infant death within 12 hours of birth, and their associated autopsy findings, were compared to 586 systematically selected successful pregnancies and their associated placental findings. Lung tissue was examined for neutrophils in pulmonary alveoli and placental tissue for acute inflammation.

Amniotic fluid infection syndrome, defined as congenital pneumonia (neutrophils found in pulmonary alveoli) associated with acute inflammation of the extraplacental fetal membranes, acute funisitis, and acute inflammation of the chorionic plate of the placenta, was identified as the prime diagnosis responsible for death in 339 cases (22 per 1000 live births). Factors associated with amniotic fluid infection syndrome included low water use, low family income (except when water use was high), lack of prenatal care, low maternal education, and heavy physical labour. The organisms isolated in affected infants and in controls were:

	Affected placenta	lungs	Controls placenta
<i>Mycoplasma</i> T-strains	26%	44%	6%
<i>E. coli</i>	20%	13%	4%
<i>Acinetobacter</i> spp.	16%	11%	3%
<i>S. epidermidis</i>	15%	13%	5%
<i>P. aeruginosa</i>	11%	6%	1%
<i>Streptococcus</i> (not Groups A, B, or D)	11%	10%	2%
<i>Enterobacter</i> spp.	11%	7%	1%

These differences were statistically significant. With the exception of mycoplasma T-strains, this distribution of organisms is similar to that found in neonatal septicaemia in developing countries. The methods used for bacterial aerobic and anaerobic cultures and isolation of *Mycoplasma* T-strains were fully described. Separate data on etiology for stillbirths and early neonatal deaths were not presented. The authors noted that local chorioamnionitis appears to be a common event, occurring in 31% of the controls in this series, but that extension in the amniotic fluid, subsequent aspiration by the fetus, and resultant congenital pneumonia occurs in only a minority of such patients. These findings may have relevance for the prevention of perinatal death and premature delivery, as well as early and appropriate treatment of affected neonates.

Ohlsson A, Serenius F.
Neonatal septicaemia in Riyadh, Saudi Arabia.
Acta Paediatr Scand, 1981; 70: 825-829.

Ohlsson A, Bailey T, Takieddine F.
Changing etiology and outcome of neonatal septicaemia in Riyadh, Saudi Arabia.
Acta Paediatr Scand, 1986; 75: 540-544.

The purpose of these papers was to describe the etiology of septicaemia, and factors associated with outcome, among neonates admitted to a modern neonatal unit in the Middle East.

All infants under 28 days old, with a positive blood culture and clinical signs of septicaemia admitted to the King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia, over an eight-year period (four years for each report), were studied. Neither the methods used for bacterial culture nor those used for antimicrobial sensitivity testing were described. Both infants born in the hospital and admissions from other hospitals were included.

During the first and second study periods, 29 and 49 neonates with septicaemia, respectively, were observed, 5 among the 2469 live births in the hospital (2 per 1000) during the first period (24 referred from other hospitals) and 8 among the 3157 infants born in the hospital (2.5 per 1000) during the second study period (39 from other hospitals, 2 from home). The distribution of bacteria isolated from blood cultures, infant characteristics, and mortality were:

	1976-1980	1980-1984
<i>Klebsiella, Serratia</i>	8 (28%)	11 (21%)
<i>E. coli</i>	4 (14%)	9 (17%)
<i>S. aureus</i>	3 (10%)	4 (8%)
Group B <i>Streptococcus</i>	0 (0%)	3 (6%)
<i>S. epidermidis</i>	0 (0%)	3 (6%)
<i>S. viridans</i>	1 (3%)	3 (6%)
<i>S. pneumoniae</i>	-	2 (4%)
<i>Salmonella enteritidis</i> spp.	9 (31%)	2 (4%)
<i>P. aeruginosa</i>	2 (7%)	2 (4%)
Total isolates	29	53
Male to female ratio	1.07:1	1.23:1
Premature	45%	47%
Mortality	45%	33%

The majority (89%) of salmonella isolated in the first time period were sensitive to gentamicin; all were resistant to ampicillin. The changes in etiological agents from the first to second time periods included a decline in the proportion of cultures positive for salmonella and the isolation of Group B streptococcus for the first time. A single isolate of *H. influenzae* was found in the second time period. The authors noted that the major pathogens in neonatal sepsis had become similar to those found in developed Western countries, except for the continuing presence of *Salmonella* species. They concluded that it was important to frequently review the etiological organisms of neonatal septicaemia in each geographical area.

Omene JA.

Neonatal septicaemia in Benin City, Nigeria: a review of 74 cases.

Trop Geogr Med, 1979; 31: 35-39.

Okolo AA, Omene JA.

Changing pattern of neonatal septicaemia in an African city.

Ann Trop Paediatr, 1985 Sep; 5(3): 123-126.

These studies were performed in order to determine the causative organisms of septicaemia, and their pattern of antimicrobial sensitivity, in the neonatal unit at the University of Benin Teaching Hospital, Benin City, Nigeria, to identify predisposing factors and major presenting symptoms and signs, and to review antibiotic effectiveness. The former study covered a three-year period ending in 1977, while the latter covered a five-and-a-half-year period ending in 1983.

Neonatal septicaemia was observed in 42 infants among 6903 live births at the hospital (6.1 per 1000) in the first period and 88 infants among 15 679 live births (5.6 per 1000) in the second period. In addition, 32 and 99 septic neonates were referred to the neonatal unit from outside the hospital in the first and second periods, respectively. The predominant organisms isolated from blood cultures, infant characteristics, and mortality were:

	1974-1977	1978-1983
<i>S. aureus</i>	18 (24%)	50 (22%)
<i>Klebsiella</i> spp.	8 (11%)	38 (17%)
<i>Pseudomonas</i> spp.	5 (7%)	34 (15%)
Coliforms	-	24 (11%)
<i>S. epidermidis</i>	3 (4%)	23 (10%)
<i>E. coli</i>	25 (34%)	21 (9%)
<i>S. pneumoniae</i>	5 (7%)	-
Total isolates	74	224
Male to female ratio	2:1	1.6:1
Premature	51%	not given
Mortality	42%	31%

The methods used for bacterial culture were not described in the former report. They were described in the latter report, but it was not noted if they included the earlier time period. It was not possible to tell from the description of the methods if isolation of *S. pneumoniae*, *H. influenzae*, or Group B streptococci was likely.

In the earlier time period, all gram negative bacteria were sensitive to gentamicin, while in the later period, only 76% of *E. coli* and 85% of *Pseudomonas* were sensitive. Respiratory difficulty, jaundice, lethargy, fever, hypothermia, diarrhoea, abdominal distension, and poor feeding were common presenting signs. However, no comparison was made with control infants or suspected but culture-negative infants. The authors concluded that there should be continuous bacterial surveillance of neonatal units in order to detect changes in the prevalence of pathogens and in the susceptibility of organisms to commonly used antibiotics.

Stagno S, Brasfield DM, Brown MB, Cassell GH, Pifer LL, Whitley RJ, Tiller RE.
Infant pneumonitis associated with cytomegalovirus, chlamydia, pneumocystis, and ureaplasma: a prospective study.
Pediatrics, 1981; 68(3): 322-329.

Brasfield DM, Stagno S, Whitley RJ, Cloud G, Cassell G, Tiller RE.
Infant pneumonitis associated with cytomegalovirus, chlamydia, pneumocystis, and ureaplasma: follow-up.
Pediatrics, 1987; 79(1): 76-83.

The former study (Stagno et al) was performed to investigate the specific infectious agents, particularly fastidious pathogens and viruses, causing pneumonia within the first three months of life, define the clinical and laboratory characteristics of these illnesses, and ascertain the nature and severity of combined infections. The methods used for isolation of the above agents were fully described. Seroconversion was considered diagnostic of infection with chlamydia and respiratory syncytial virus. The latter study (Brasfield et al) investigated the clinical course and long-term outcome of these infections according to the etiological agent.

Over a seven-year period, at The Children's Hospital, Birmingham, Alabama, USA, 205 infants between the ages of 2 and 12 weeks with cough, tachypnoea, retractions, and radiographic evidence of bilateral diffuse pulmonary infiltrates with air trapping were studied. Infants with other causes of respiratory symptoms, including lobar or aspiration pneumonia, were excluded. Control infants, with sex and racial distribution similar to the study infants, were selected among infants hospitalized for reasons other than pneumonia.

Among 205 infants with pneumonitis, 145 (70%) had evidence of infection with one or more agent. The distribution of agents was:

	Study infants		Control infants	
<i>Chlamydia trachomatis</i>	61/193	(32%)		
Respiratory syncytial virus	33/142	(23%)		
Cytomegalovirus	42/203	(21%)	3/97	(3%)
<i>Pneumocystis carinii</i>	30/171	(18%)		
<i>Ureaplasma urealyticum</i>	21/125	(17%)	2/49	(4%)
Enterovirus	10/135	(7%)		
Adenovirus	7/135	(5%)		
Parainfluenza	7/135	(5%)		
<i>Mycoplasma hominis</i>	3/125	(2%)	1/49	(2%)
Total positive findings	145/205	(70%)	6/113	(5%)
Multiple agents	55/145			

The differences between study and control infants were statistically significant for cytomegalovirus and *U. urealyticum*. Among the study infants, cough was found in 56% and elevated temperature in 8%. Rales were noted in 74% and wheezing in 34%. There was no specific radiographic pattern for any of the organisms involved. Follow-up of study infants, reported in the latter paper, demonstrated recurrent wheezing episodes in 46%, persistently abnormal chest radiographs for at least one year in 15%, and abnormal pulmonary functions in 15 of 25 (60%) children 6 to 7 years of age.

The data confirmed the role of pathogens requiring special isolation techniques in the etiology of pneumonia in young infants and demonstrated long-term sequelae from these infections. The role of *P. carinii* and *U. urealyticum* as etiological agents of pneumonia in previously well young infants remained controversial.

Chapter 6: The young infant under 2 months of age

Section B: Normal respiratory rate

Introduction

The basis of certainty about the significance of pathological findings lies generally in the comparison with normal findings. Four reports on respiratory rate in healthy young infants have been selected for this section. These reports deal with the range, determinants and variability of respiratory rates found at different ages in full term normal infants. Many of these reports deal with mechanical measures in sleeping infants, which may not allow direct extrapolation to the clinical situation. However, one report includes awake infants and a second includes recordings taken over 24 hours. The extent to which mechanical measurements differ from direct observation of the respiratory rate has not been well studied. As with most biological parameters, no clear cutoff appears from these data to distinguish health from disease, but, together with findings in ill infants (found in the following section, Clinical detection) informed choices can be made about persistently elevated respiratory rates above which suspicion of pathology is high.

An additional paper on this subject will be annotated in Volume II of this series as it was published in 1991: Simoes AEF, Roark R, Berman S, Esler LL, Murphy J. **Respiratory rate: measurement of variability over time and accuracy at different counting periods.** *Arch Dis Child*, 1991; 66: 1199-1203.

Ashton R, Connolly K.

The relation of respiration rate and heart rate to sleep states in the human newborn.

Develop Med Child Neurol, 1971; 13: 180-187.

This study was performed in order to investigate the reproducibility of a newborn's heart rate and respiratory rate at different times while in the same state, including rapid eye movement (REM) and non-REM sleep.

At the Jessop Hospital for Women, Sheffield, UK, respiratory rate and heart rate were monitored in 22 unstimulated healthy full term newborns, aged 2-6 days (mean 3 days), immediately after feeding. There were 12 males and 10 females. All measurements and observations were made while the infant lay in a crib within a sound-attenuating chamber, with standardized temperature (30°C) and lighting. A mercury-in-rubber strain gauge fixed around the lower chest region was used to monitor respiration and the electrocardiogram signal was picked up from a standard 3-electrode array. Sleep states were determined by observation criteria without the use of electroencephalogram (EEG) recordings.

The recordings averaged three hours, and in most cases included three or more sleep cycles. The interobserver reliability for judging sleep states was high (98% agreement). The mean values for respiratory rate per minute, and the standard deviation (SD) for each, in three subsequent sleep cycles were:

NREM sleep:	mean	45	43	43
	<u>±SD</u>	10	9	13
REM sleep:	mean	54	48	47
	<u>±SD</u>	11	9	9

There was a significant overall decrease in respiration rate as the interval since the last feed increased. Despite these changes over time within a sleep state, a marked difference between the two different sleep states remained. This study provides useful data on the variability, normal range, and determinants of the respiratory rate in the sleeping newborn.

Curzi-Dascalova L, Gaudebout C, Dreyfus-Brisac C.

Respiratory frequencies of sleeping infants during the first months of life: correlation between values in different sleep states.

Early Human Development, 1981; 5: 39-54.

The purpose of the study was to investigate the normal respiratory rate in young infants.

At the Port Royal Hospital, Paris, France, respiratory rates in quiet and active sleep were measured between feedings in the morning or around noon for at least one sleep cycle in 57 normal infants, 22 full term newborns and 35 infants aged 2-18 weeks. All babies came from normal pregnancies, had uneventful deliveries, and their further development was normal. The infants aged 2-18 weeks were staying in a residential nursery, either permanently or only during the day. Measurements were taken of the electroencephalogram (EEG), eye movements, and thoracic respiratory movements (using a graphite rubber strain gauge) with the babies sleeping in the supine position, normally dressed, and at room temperature of 25 to 26°C. Quiet and active sleep were differentiated by rapid eye movements, body movements, EEG pattern, and regularity of the respiratory rate.

The mean values for respiratory rate measurements per minute, and standard deviations (SD), at different ages were:

Age	n	Quiet sleep		Active sleep	
		mean	<u>±SD</u>	mean	<u>±SD</u>
2-10 days	22	36	7	48	9
2-5 weeks	1	50	11	64	14
6-10 weeks	14	46	11	57	16
11-18 weeks	10	38	10	43	10

Respiratory rate varied significantly according to the sleep state (higher in active sleep), the age of the infant (highest at 2-5 weeks and 6-10 weeks), and by individual infants. The authors also reviewed 12 other studies of the respiratory rate in normal infants and 5 studies in pathological infants. They presented evidence from these studies that respiratory rates of 59, 62, and 57 have been found in active daytime sleep in normal newborns, and it was their opinion that normal values of 30-40/min for newborns, found in textbooks, were too low.

Hoppenbrouwers T, Harper RM, Hodgman JE, Sterman MB, McGinty DJ.

Polygraphic studies of normal infants during the first six months of life. II. Respiratory rate and variability as a function of state.

Pediat Res, 1978; 12: 120-125.

In order to investigate the spontaneous respiratory rate and its variability as a function of age and sleep state, 8 full term infants, 5 females and 3 males, were examined using 12 hour monitoring sessions at the Los Angeles County-University of California Medical Centre, Los Angeles, California, USA. The infants were full term, of appropriate birth weight for gestational age, had one minute Apgar scores of 8 or 9, and were neurologically normal. Each infant was admitted to the sleep laboratory for an all night monitoring session during the first week of life and at 1, 2, 3, 4, and 6 months of age. Under standardized conditions of light (darkened room) and temperature (23-25°C), with newborn infants swaddled and arm restraints applied to older infants, monitoring took place by electroencephalogram (EEG), impedance pneumography for chest or abdominal excursions, carbon dioxide measurement of expired air, and television recording. The sleep state was coded by trained personnel as quiet sleep, active sleep, awake, or indeterminate, relying partially on the respiratory pattern, especially the regularity of breathing.

The mean values for respiratory rates per minute, and standard deviations (SD), at different ages were:

	Mean 1 week \pm SD	Mean 2 months \pm SD	Mean 6 months \pm SD
Quiet sleep	38 9	30 5	24 4
Active sleep	50 8	36 6	28 4
Awake	50 10	48 7	43 10
Indeterminate	47 10	37 8	28 6

Individual differences in respiratory rate were large, especially during the first two months. The highest values at one week of age, 53 (quiet sleep), 65 (active sleep), 68 (awake), and 70 (indeterminate) were found in the same infant, while the lowest values of 27, 41, 43, and 41, respectively, were found in one of two infants. Respiratory rates were found to be highest during the first week of life, then declined during the next two months and began to level out at 3 months of age. Respiratory rate and variability were greatest when the infant was awake, lowest during quiet sleep, and intermediate during active sleep.

Richards JM, Alexander JR, Shinebourne EA, de Swiet M, Wilson AJ, Southall DP.
Sequential 22-hour profiles of breathing patterns and heart rate in 110 full-term infants during their first 6 months of life.
Pediatrics, 1984; 74(5): 763-777.

In order to investigate the heart rate and breathing pattern in infants, sequential 24-hour recordings at 1 week, 6 weeks, 3 months, and 6 months of age were obtained from 110 full-term infants at Brompton Hospital, London, UK. Most pregnancies and deliveries were unremarkable. There were 56 boys and all but 7 infants were considered of appropriate weight for gestational age. Recordings of heart rate and respiratory rate (from an abdominal wall movement detector) were made at home in all infants after 15 days of age. The mean duration of each recording was 22 hours. Sleep states, environmental conditions, and relation of respiratory rate to feeding were not recorded.

The number of recordings, the means values for respiratory rate per minute, and the standard deviation (SD) at different ages were:

Age	Number	Mean	\pm SD
1-3 days	26	40	8
4-7 days	36	43	16
1-2 weeks	24	45	8
4-6 weeks	41	38	6
7-9 weeks	50	37	6
10-20 weeks	97	31	6
20-30 weeks	91	27	4

The respiratory rate decreased progressively after 4 weeks of age. The number and duration of pauses and the amount of periodic breathing also decreased with age. The largest variability in respiration occurred in the first two weeks of life.

Chapter 6: The young infant under 2 months of age

Section C: Clinical detection

Introduction

Assessment of the sick young infant is one of the most critical and challenging skills in clinical medicine; clinical signs are often nonspecific, progression can be rapid, and mortality is high. Low birth weight, prematurity, congenital anomalies and infections, complications of labour and delivery, and other conditions early in life such as transient tachypnoea or metabolic abnormalities often affect the clinical presentation. As with etiology, the clinical presentation of serious illness varies considerably with age, particularly within the first week of life. This section contains a summary table of clinical outcomes in febrile young infants reported from developed countries. It also contains annotations of studies reporting on the performance of the overall clinical impression, a study of clinical outcomes in young infants with a history of fever but afebrile at the time of presentation, a study of the usefulness of respiratory distress for identifying pneumonia, and three reports from the same institution on routine monitoring of the respiratory rate in postnatal wards.

Data from developing countries (see Section A: Etiology) on clinical signs in the age group from 4 to 8 weeks are scant, and very little has been reported about clinical outcomes or prediction of risk based on enrolment of infants with fever. The reports summarized on the table used different methods for patient selection (ages, definition of fever, ambulatory versus hospitalized patients, exclusions for prematurity or congenital conditions) and different standards for assessing and categorizing the severity of illness. However, in the settings of these studies, fever as a presenting complaint in infants under 3 months of age appears to be relatively rare, especially in the younger ages. Among young infants presenting with fever, lower respiratory infection was found more frequently than any other condition, with the exception of aseptic meningitis.

The performance of criteria for identifying infants at risk for serious disease has been investigated in several settings in developed countries. In these studies, the best predictor of septicaemia appears to be the overall clinical impression, but the nature of the overall clinical impression and the ability to train physicians and other health workers in these skills remains unclear. The majority of these studies demonstrate excellent sensitivity of the overall clinical impression in identifying infants with septicaemia, but sensitivities as low as 67% and 91% were also found. The results of studies of clinical signs now in progress in developing countries may help to further clarify the clinical signs, individually or combined, which most accurately predict the need for rapid intervention and management at a referral facility.

Summary table of studies considering the significance of fever in young infants

First author	Place	Study type	Study size	Upper age limit months	Definition of fever	LRI	Sept	Bact Mening	Otit	UTI	Asept mening	Focal bact infect	*Total infections (%)
McCarthy 1976	New Haven U.S.A.	prospec	22	3	104°F (40°C)	3	0	3	2	0	1	0	9 41%
Roberts 1977	Baltimore U.S.A.	prospec	61	2	38°C	4	9	2	7	0	5	0	27 44%
O'Shea 1978	Providence U.S.A.	prospec	33	3	100.5°F (38°C)	0	3	1	0	0	0	0	4 12%
Pantell 1980	Charleston U.S.A.	retrospec	12	3	38.3°C	0	0	1	3	0	0	0	4 33%
Greene 1981	Nashville U.S.A.	combined	183	2	37.8°C	39	1	1	28	4	26	9	108 59%
Crain 1982	Bronx U.S.A.	prospec	175	2	38°C	13	6	2	24	1	26	7	79 45%
Voorra 1982	Chicago U.S.A.	prospec	100	4 days	37.8°C	1	6	3	0	1	0	2	13 13%

Summary table of studies considering the significance of fever in young infants

First author	Place	Study type	Study size	Upper age limit months	Definition of fever	LRI	Sept	Bact Mening	Otit	UTI	Asept mening	Focal bact infect	*Total infections (%)
Caspe 1983	Bronx U.S.A.	prospec	305	2	38°C	5	11	3	8	9	15	14	65 21%
DeAngelis 1983	Baltimore U.S.A.	retrospec	190	2	38°C	14	1	7	13	4	40	11	90 47%
Leggiadro 1983	E. Meadow U.S.A.	retrospec	27	2	suspected sepsis	0	2	0	0	2	1	1	6 22%
Klein 1984	Boston U.S.A.	retrospec	187	3	37.7°C	27	3	0	28	3	5	3	69 37%
Berkowitz 1985	Los Angeles Irvine San Diego U.S.A.	retrospec	434	2	38°C	66	9	7	16	4	58	2	162 37%
Dagan 1985	Rochester U.S.A.	prospec	233	3	suspected sepsis	51	9	0	13	4	39	8	124 53%
Krober 1985	Honolulu U.S.A.	prospec	182	3	38°C	10	0	1	17	20	54	7	109 60%
Rosenberg 1985	Detroit U.S.A.	prospec	122	2	37.8°C	4	5	1	16	0	11	1	38 31%

Summary table of studies considering the significance of fever in young infants

First author	Place	Study type	Study size	Upper age limit months	Definition of fever	LRI	Sept	Bact Mening	Otit	UTI	Asept mening	Focal bact infect	*Total infections (%)
Anbar 1986	Boston U.S.A.	retrospec	117	3	38°C	0	6	0	15	7	0	3	31 26%
Bonadio 1987	Milwaukee U.S.A.	retrospec	109	1	history or 38°C	4	1	2	0	7	0	2	16 15%
King 1987	Baltimore U.S.A.	combined	342	2	38°C	15	13	9	26	7	49	18	137 40%
Crain 1988	Bronx U.S.A.	prospec	46	0.5	38.1°C	3	1	3	4	5	7	4	27 59%
Dagan 1988	Beer-Sheva Israel	prospec	237	2	38°C	20	9	1	7	8	0	6	51 22%
Heulitt 1988	New York U.S.A.	retrospec	192	3	100.5°F (38°C)	12	5	2	21	13	10	5	68 35%
Losek 1989	Milwaukee U.S.A.	combined	257	2	history or 38.3°C	19	13	3	25	11	43	0	114 44%
Baker 1990	Philadelphia U.S.A.	prospec	126	2	38.2°C	11	4	0	4	5	18	2	44 35%

Summary table of studies considering the significance of fever in young infants

First author	Place	Study type	Study size	Upper age limit months	Definition of fever	LRI	Sept	Bact Mening	Otit	UTI	Asept mening	Focal bact infect	*Total infections (%)
Bonadio 1990	Milwaukee U.S.A.	retrospec	292	2	history or 38°C	41	8	4	6	9	15	5	88 30%
Broner 1990	Tampa U.S.A.	prospec	52	2	38.1°C	9	5	0	11	1	5	2	33 63%
Wasserman 1990	Honolulu U.S.A.	retrospec	443	3	38°C	17	8	6	74	34	50	10	199 45%
Total			4626			404 9%	139 3%	62 1%	374 8%	159 3%	480 10%	122 3%	1740 38%

LRI = pneumonia, bronchiolitis Otit = otitis media Prospec = prospective study

Sept = positive bacterial culture in an infant with clinical features suggesting septicaemia UTI = urinary tract infection Retrospec = retrospective chart review

Bact mening = bacterial meningitis Asept mening = aseptic meningitis Combined = retrospective combined with prospective

Focal bact infect = cellulitis, omphalitis, septic arthritis, osteomyelitis, bacterial gastroenteritis

*Total infect = total number of listed infections, including multiple infections in the same child

References for the summary table of studies considering the significance of fever in young infants

* Indicates report annotated in this section

McCarthy PL, Jekel JF, Dolan TF. Temperature greater than or equal to 40°C in children less than 24 months of age: a prospective study. *Pediatrics*, 1976; 59(5): 663-668.

Roberts KR, Borzy MS. Fever in the first eight weeks of life. *Johns Hopkins Medical Journal*, 1977; 141: 9-13.

O'Shea JS. Assessing the significance of fever in young infants. *Clinical Pediatrics*, 1978; 17(11): 854-856.

Pantell RH, Naber M, Lamar R, Dias JK. Fever in the first six months of life: risks of underlying serious infection. *Clin Pediatr*, 1980; 19(2): 77-82.

Greene JW, Hara C, O'Connor S, Altemeier WA. Management of febrile outpatient neonates. *Clin Pediatr*, 1981; 20(6): 375-380.

* Crain EF, Shelov SP. Febrile infants: predictors of bacteraemia. *J Pediatr*, 1982; 101(5): 686-689.

Voora S, Srinivasan G, Lilien LD, Yeh TF, Pildea RS. Fever in full-term newborns in the first four days of life. *Pediatrics*, 1982; 69(1): 40-44.

* Caspe WB, Chamudes O, Louie B. The evaluation and treatment of the febrile infant. *Pediatr Infect Dis J*, 1983; 2(2): 131-135.

DeAngelis C, Joffe A, Wildon M, Willis E. Iatrogenic risks and financial costs of hospitalizing febrile infants. *Am J Dis Child*, 1983; 137: 1146-1149.

Leggiadro RJ, Darras BT. Viral and bacterial pathogens of suspected sepsis in young infants. *Pediatr Infect Dis J*, 1983; 2(4): 287-289.

Klein JO, Schlesinger PC, Karasic RB. Management of the febrile infant three months of age or younger. *Pediatr Infect Dis J*, 1984; 3(1): 75-79.

Berkowitz CD, Uchiyama N, Tully SB, Marble RD, Spencer M, Stein MT, Orr DP. Fever in infants less than two months of age: spectrum of disease and predictors of outcome. *Pediatric Emergency Care*, 1985; 1(3): 128-135.

* Dagan R, Powell KR, Hall CB, Menegus MA. Identification of infants unlikely to have serious bacterial infection although hospitalized for suspected sepsis. *J Pediatr*, 1985; 107(6): 855-60.

Krober MS, Bass JW, Powell JM, et al. Bacterial and viral pathogens causing fever in infants less than 3 months old. *Am J Dis Child*, 1985; 139: 889-892.

Rosenberg N, Vranesich P, Cohen S. Incidence of serious infection in infants under age two months with fever. *Pediatric Emergency Care*, 1985; 1(2): 54-56.

- * Anbar RB, Richardson-de Corral V, O'Malley PJ. Difficulties in universal application of criteria identifying infants at low risk for serious bacterial infection. *J Pediatr*, 1986 Sep; 109(3): 483-485.
- * Bonadio WA. Incidence of serious infections in afebrile neonates with a history of fever. *Pediatr Infect Dis J*, 1987; 6(10): 911-914.
- * King JC, Berman ED, Wright PF. Evaluation of fever in infants less than 8 weeks old. *South Med J*, 1987; 80(8): 948-952.

Crain EF, Gershel JC. Which febrile infants younger than two weeks of age are likely to have sepsis? A pilot study. *Pediatr Infect Dis J*, 1988; 7(7): 561-564.

Dagan R, Sofer S, Phillip M, Shachak E. Ambulatory care of febrile infants younger than 2 months of age classified as being at low risk for having serious bacterial infections. *J Pediatr*, 1988; 112(3): 355-360.

- * Heulitt MJ, Ablow RC, Santos CC, O'Shea TM, Hilfer CL. Febrile infants less than 3 months old: value of chest radiography. *Radiology*, 1988; 167(1): 135-137.

Losek JD, Kishaba G, Berens RJ, Bonadio WA, Wells RG. Indications for chest roentgenogram in the febrile young infant. *Pediatric Emergency Care*, 1989; 5(3): 149-152.

Baker MD, Avner JR, Bell LM. Failure of infant observation scales in detecting serious illness in febrile, 4- to 8-week old infants. *Pediatrics*, 1990; 85(6): 1040-1043.

Bonadio WA, Hegenbarth M, Zachariason M. Correlating reported fever in young infants with subsequent temperature patterns and rate of serious bacterial infections. *Pediatr Infect Dis J*, 1990; 9(3): 158-160.

Broner CW, Polk SA, Sherman JM. Febrile infants less than eight weeks old. Predictors of infection. *Clin Pediatr*, 1990; 29(8): 438-443.

Wasserman GM, White CB. Evaluation of the necessity for hospitalization of the febrile infant less than three months of age. *Pediatr Infect Dis J*, 1990; 9(3): 163-169.

Anbar RD, Richardson-de Corral V, O'Malley PJ.

Difficulties in universal application of criteria identifying infants at low risk for serious bacterial infection.

J Pediatr, 1986; 109(3): 483-485.

In order to evaluate previously reported low risk criteria (Dagan et al, below), a chart review of all infants under three years of age with acute febrile illness (temperature over 38°C rectally) seen at the Massachusetts General Hospital Pediatric Emergency Ward, Boston, Massachusetts, USA, over a one-year period was performed. According to the defined criteria, an infant was categorized as low risk if there was no evidence of soft tissue, skeletal, or ear infection on physical exam and if the white cell and band counts and urinalysis were normal.

Infants were excluded if a blood culture was not drawn, if they had received antibiotics prior to presentation, or if they had been ill subsequent to their discharge from the hospital after their birth. All infants were investigated for septicaemia, including lumbar puncture in most (94%). Bacterial infections considered serious included bacteraemia, meningitis, cellulitis, gastroenteritis, and urinary tract infection. Dagan et al (see below) also included osteomyelitis in this list.

The male to female ratio and breakdown by age of the 117 study infants was not given. Among 70 infants meeting the low risk criteria, 3 (4%) had serious bacterial infection compared with 9 (19%) of 47 infants in the high risk group. Two (3%) of the infants in the low risk group had bacteraemia, compared with 4 (9%) in the high risk group. The sensitivity, specificity, and positive predictive value of the risk criteria for serious bacterial infection were 75%, 64%, and 19%, respectively, and for bacteraemia 67%, 61%, and 9%, respectively. The number of infants with pneumonia or the number with specific clinical signs was not reported. Additional or alternative criteria could not be identified that would help to distinguish a low risk group.

The performance of the low risk criteria are poorer in this study than in Dagan's group of patients, but patient selection was not identical (premature infants, infants with perinatal complications, and outpatients were not excluded in this study, and afebrile infants were excluded), and this study was carried out retrospectively. The authors noted that low risk criteria should not allow inclusion of any infants with serious bacterial infection, particularly when the incidence of serious bacterial infection is low, as it was in this group of febrile infants (10%, the same as Dagan et al). They concluded that they were unable to define predictors of low risk from their patient data.

Berman S, Shanks MB, Feiten D, Horgan G, Rumack C.
Acute respiratory infections during the first three months of life: clinical, radiologic and physiologic predictors of etiology.
Pediatr Emerg Care, 1990; 6(3): 179-182.

The study was performed to investigate the clinical characteristics, radiological findings, and oxygen saturation of specific respiratory infections during early infancy.

Over a 25-month period, infants 2-12 weeks of age delivered vaginally and presenting during daytime hours to the University Hospital clinic, Denver, Colorado, USA, with cough, congestion, or rhinorrhoea were enrolled. Since enrolment was not consecutive, the authors noted that it was possible that infants with signs of respiratory distress were more likely to be referred for enrolment than those with minimal respiratory signs. Chest X-rays, obtained in 66 of 90 (73%) study infants, were read by two paediatric radiologists without clinical information. A radiological diagnosis of pneumonia was reached when findings included diffuse interstitial infiltrate, two or more subsegmental parenchymal infiltrates, segmental parenchymal infiltrates, or lobar opacification. Laboratory investigations included nasopharyngeal aspirate for viral culture and respiratory syncytial virus (RSV) immunofluorescence during the RSV season, *Chlamydia* culture and immunofluorescence, and pertussis culture and immunofluorescence.

The mean age of the study population was 6.8 weeks; 32 infants were under 5 weeks of age, 38 were 5-8 weeks, and 20 were 9-12 weeks. The male to female ratio was 1.4:1 and 16% were born prior to 38 weeks' gestation. RSV was identified in 25 children, *Chlamydia* in 16, parainfluenza in 6, rhinovirus in 3, pertussis in 2, and cytomegalovirus in 1. Blood cultures were taken in 32 hospitalized infants (36%), but none was positive. No clinical characteristics in the history (cough, congestion, rhinorrhoea, apnoea, maternal sexually transmitted disease) or physical examination (respiratory rate, retractions, observed cough, wheezing, rales, conjunctivitis, diminished breath sounds, fever, grunting) helped to distinguish children with a particular organism. X-ray findings could not distinguish between infants with or without an etiological agent or between agents. Hospitalization was significantly associated with RSV and *Chlamydia* infection, despite the lack of etiological information at the time decisions were made about hospitalization. Oxygen saturation, obtained in 30 infants (33%), correlated with retractions (sensitivity 75%, specificity 71%) but not with the respiratory rate.

The data indicate that neither clinical signs nor radiography can accurately distinguish viral pathogens from *Chlamydia* or from each other, and that retractions may be the most useful clinical sign for the presence of oxygen desaturation. These findings need to be extrapolated with care to developing country settings where the etiology of lower respiratory infections among young infants may be different.

Bonadio WA.

Incidence of serious infections in afebrile neonates with a history of fever.

Pediatr Infect Dis J, 1987; 6(10): 911-914.

The study was conducted to evaluate whether the neonate with a history of fever who is afebrile at the time of evaluation is at risk of serious bacterial infection and whether laboratory and clinical indices are accurate in distinguishing those who have serious infection from those who do not.

Over a six-month period, 109 consecutive full term previously well infants younger than 4 weeks of age, reported to be febrile at home within 24 hours of admission to the Emergency Department of the Children's Hospital of Wisconsin, Milwaukee, Wisconsin, USA, were identified. All were evaluated for sepsis and were considered to have a serious infection if a bacterial pathogen was isolated from culture of cerebrospinal fluid (CSF), blood, urine, or stool for which hospitalization and parenteral antibiotics were indicated. Infants with hypothermia and current antibiotics or antipyretics (if afebrile at the time of evaluation) were excluded. All study infants had a complete blood count and blood cultures, but not all had CSF culture (91%), urinalysis (85%), chest radiograph (77%), or urine culture (75%).

Among the study infants, 54 (50%) were afebrile at the time of admission to the emergency department. None had a focal source of infection and none was found to have a serious infection (as defined above), but four had a pulmonary infiltrate on the chest radiograph. Of 55 infants with documented fever over 38°C, 8 were found to have a serious bacterial infection including 3 with urinary tract infections (>100 000 colony forming units/ml of *E. coli*), 2 Group B *Streptococcus* meningitis, 2 *Salmonella* gastroenteritis, and 1 *Salmonella* bacteraemia. The rate of serious bacterial infection was significantly different in the febrile (15%) and afebrile (0%) groups but if pneumonitis was included as a serious infection, the difference diminished (15% versus 7%) and was no longer statistically significant.

The data suggest that previously well young infants with a history of fever but who were afebrile at the time of assessment, and who did not receive antipyretics, have a low risk for serious bacterial infection. However, this study was a retrospective review in which not all study children received all tests. Thus, serious bacterial infections may have been missed in a few children. Also, bacterial infection could not be ruled out in 4 children with pulmonary infiltrates, despite negative blood cultures.

Caspe WB, Chamudes O, Louie B.
The evaluation and treatment of the febrile infant.
Pediatr Inf Dis, 1983; 2(2): 131-135.

To investigate the premise that small infants are at increased risk for developing bacteraemia, all infants under 60 days of age with rectal temperatures of 38°C or more seen at the Bronx-Lebanon Hospital Outpatient Department, Bronx, New York, USA, over a five-and-a-half-year period, were studied. All 305 study infants, constituting 0.1% of the total visits, were admitted. After the history and physical exam, the paediatric resident recorded if the baby appeared to be ill, based on inconsolability when held or fed, or unresponsiveness to the environment. All study infants were investigated for sepsis. Blood cultures positive for *S. epidermidis* were considered to be contaminated and were disregarded.

In the study group of 305 infants, the male to female ratio was 1.2:1. The discharge diagnoses consisted of: 256 (84%) presumed viral illness; 32 (10%) proven bacterial illness including 11 (4%) sepsis/meningitis; 4 (1%) pneumonia; 8 (3%) otitis media; and 5 (2%) other illnesses. There were 96 infants judged to appear ill, including all 3 infants with pneumonia and 10 of 11 with bacteraemia. The sensitivity, specificity, and positive predictive value of ill appearance were 91%, 71%, and 10%, respectively, for bacteraemia at all ages studied. The sensitivity of ill appearance was 100% among infants over 30 days of age. The mean temperature of infants with bacteraemia was significantly higher than that for infants without bacteraemia, but there was no specific temperature above which bacteraemia was more likely to occur. Bacteraemia was found in 7 of 107 (6%) infants under 30 days of age and 4 of 198 (2%) of infants aged 30 to 60 days, but the difference was not statistically significant. Of all infants enrolled, 21% had significant disease (aseptic meningitis, bronchiolitis, bacterial infections, otitis media, pneumonia, or narcotic withdrawal syndrome) and 4% had bacteraemia.

The authors concluded that the appearance of the infant, as judged by the paediatric resident, proved to be the most sensitive indicator of bacteraemia.

Cowen J, Gordon H, Sanderson PJ, Valman HB.
Group B streptococcal infection in a maternity unit.
British Journal of Obstetrics and Gynecology, 1978; 85: 541-545.

Valman HB, Wright BM, Lawrence C. **Measurement of respiratory rate in the newborn.**
Brit Med J, 1983; 286: 1783-1784.

Mifsud A, Seal D, Wall R, Valman B.
Reduced neonatal mortality from infection after introduction of respiratory monitoring.
Brit Med J, 1988; 296: 17-18.

Three reports, from Northwick Park Hospital, Harrow, UK, present the results of routine monitoring of the respiratory rate in all infants in the postnatal wards, which began in January, 1977.

The first report (Cowen et al) documented six cases of neonatal infection with Group B streptococci over an eight-month period. Two (33%) babies died. The infections included septicaemia with positive blood cultures (3 infants) or high clinical suspicion of Group B streptococcal infection with isolation of the organism from several surface sites. The onset of disease was within 12 hours for 5 infants and at 7 days for one infant. All six babies had a rapid respiratory rate and this was the first sign of disease in each case. Other signs, including chest recession, grunting, and colour change, developed later in 4 babies. The authors favoured antibiotic treatment for all infants who develop tachypnoea in the newborn period, since they found the time interval between the onset of symptoms and marked clinical deterioration to be very short, and the mortality high.

The second report (Valman, et al) presented the experience over a one-year period of routine monitoring of the respiratory rate hourly for the first twelve hours then two-hourly for the subsequent 24 hours for all infants in the postnatal wards. The respiratory rate was monitored by a hand-held monitor recording pneumatic signals from an air-filled capsule on each baby's chest. During the study period, 29 (1%) of 2789 infants admitted to the postnatal wards were transferred to the special care unit, with a raised respiratory rate (>60/min). Nine had a raised respiratory rate transiently and were given no treatment but the remaining 19, with prolonged tachypnoea (over two hours), received antibiotics. Among this last group, 4 had evidence of colonization or infection with Group B streptococci.

The third report (Mifsud et al) presented a 7-year review of 19 neonates with early onset (under 7 days of age) Group B streptococcal septicaemia. The monitoring technique and treatment protocol were similar to those described above (Valman et al). Among 19 affected neonates, tachypnoea was the first and initially the only sign of infection in 6, and was observed after blood cultures were taken for other reasons in 7. Early tachypnoea was not observed in four affected neonates and two infants developed septicaemia while being ventilated for apnoea. The incidence of neonatal septicaemia caused by Group B streptococci was three times higher than the average for the United Kingdom but only one death occurred in the 20 cases documented, a mortality rate much lower than the national average. The authors attributed these results to the early antibiotic treatment of neonates with tachypnoea.

Crain EF, Shelov SP.

Febrile infants: predictors of bacteraemia.

J Pediatr, 1982 Nov; 101(5): 686-689.

The purpose of this study was to investigate the incidence of bacteraemia in a group of young infants with fever presenting to an urban emergency room, and to determine if there were any criteria by which paediatric residents could predict bacteraemia in these infants at the time of the first examination.

Prospectively over a two-year period, 175 infants under 8 weeks of age presenting to the paediatric emergency room of the Bronx Municipal Hospital Center, Bronx, New York, USA, with rectal temperatures of 38°C or more, were studied (0.1% of total visits). All infants received a full evaluation for sepsis and were admitted for antibiotic therapy pending culture results. After the history and physical examination, the paediatric resident recorded impressions of the infant's tone, colour, activity, cry, and irritability, as well as an overall impression of the likelihood that the infant had sepsis. According to a later sampling of residents, this overall impression was based on the infant's level of activity, feeding pattern, irritability, responsiveness, and ability to be consoled.

Culture positive bacterial infections occurred in 11 (6%) infants and bacteraemia in 6 (3%). Pneumonia occurred in 11 (6%) infants, none of whom had bacteraemia. Among infants with no source identified during the first emergency room examination, temperature over 38.6°C (the median), and impression of irritability, tone, cry, and activity level during the examination were not significantly associated with bacteraemia. The impression of bacteraemia was either strong or ambivalent in all 5 infants with bacteraemia compared to 54 (42%) of the other 129 infants without an initial source identified. The sensitivity, specificity, and positive predictive value of clinical impression, among infants with no source identified at the first examination, were 100%, 58%, and 8%, respectively, for bacteraemia.

The authors concluded that an impression of sepsis was the only clinical variable significantly associated with bacteraemia. However, components of the impression of sepsis (activity and irritability) were evaluated separately and were found not to be associated with bacteraemia. The relative contribution to the impression of sepsis of feeding pattern, responsiveness, and ability to be consoled was not analysed, nor was the value of the global judgement compared to the value of its components.

Dagan R, Powell KR, Hall CB, Menegus MA.

Identification of infants unlikely to have serious bacterial infection although hospitalized for suspected sepsis.

J Pediatr, 1985 Dec; 107(6): 855-60.

The purpose of this study was to investigate prospectively the usefulness of physical examination, white blood cell and band count, and urinalysis, considered together as criteria for the identification of infants without serious bacterial infection among infants hospitalized for suspected sepsis.

Over a two-year period, 233 previously healthy infants younger than 3 months of age, admitted by house officers for evaluation of sepsis at Strong Memorial Hospital, Rochester, New York, USA, were enrolled. Approximately 10% of otherwise eligible infants were excluded because they were not considered previously well. Those bacterial infections considered serious included bacteraemia, meningitis, cellulitis, osteomyelitis, gastroenteritis, and urinary tract infection. Infants were considered at low risk for serious bacterial infection at the time of hospitalization if they had no findings consistent with a soft tissue, skeletal, or ear infection, normal white blood cell and differential counts, and normal urinalysis. Chest X-ray and cerebrospinal fluid findings were not used to assign infants to the high and low risk groups.

The male to female ratio among 233 study infants was 1.4:1 and the mean age was 38 days with a range of 4 to 89 days. Among 144 infants meeting the low risk criteria, 1 (1%) had a serious bacterial infection compared with 22 (25%) of 89 infants in the high risk group. None of the infants in the low risk group had bacteraemia; 9 (10%) in the high risk group did. The sensitivity, specificity, and positive predictive value of the risk criteria for serious bacterial infection was 96%, 68%, and 25%, respectively, and for bacteraemia 100%, 64%, and 10%, respectively. The proportion of infants with abnormal chest radiograph findings and cerebrospinal fluid pleocytosis, but negative cultures, was similar in both low and high risk groups. Irritability, lethargy, anorexia, diarrhoea or vomiting, and respiratory findings were also similar in both groups. The mean body temperature was similar in low risk and high risk infants, as well as in those with serious bacterial infection, but 15% of infants with temperatures over 39°C had serious bacterial infection, as did 24% of infants with temperatures over 40°C, compared to 10% overall.

Criteria including focal findings on the physical examination and simple laboratory examinations appeared to identify young febrile infants at low risk of serious bacterial infection in this setting. However, an assumption in this study was that infants with pneumonia and culture-negative meningitis had mild, self-limiting viral infections, an assumption which would need to be re-examined in other settings wishing to implement these or similar criteria.

Heulitt MJ, Ablow RC, Santos CC, O'Shea TM, Hilfer CL.
Febrile infants less than 3 months old: value of chest radiography.
Radiology, 1988; 167: 135-137.

This study was performed to investigate the prevalence of pneumonia in febrile infants less than 3 months old who did not have signs of respiratory distress.

Retrospectively, the records of all infants less than 3 months old, admitted to St. Luke's-Roosevelt Hospital Center, New York, USA, over a four-and-a-half-year period, with a rectal temperature greater than 100.5°F (38.1°C), were reviewed. All infants were admitted to the hospital and had a complete diagnostic evaluation for septicaemia. The presence of respiratory distress was defined as one or more of: respiratory rate >60/min, chest wall retraction, nasal flaring, rales, grunting, apnoea and/or cyanosis. Each chest radiograph was reviewed by two paediatric radiologists and classified as negative, mild, moderate, or severe, according to defined criteria.

Among 192 infants, the male to female ratio was 1.3:1. Eighty-seven were 30 days old or less, 76 were 31-60 days old, and 29 were 61-89 days old. The most common final diagnoses were: fever without source (20%), upper respiratory tract infection (20%), viral syndrome (12%), otitis media (11%), gastroenteritis (8%), urinary tract infection (7%), and pneumonia (6%). Bacteraemia was found in 5 (3%) infants. Positive radiographs were found in 12 (6%) infants, 7 of whom had signs of respiratory distress. The sensitivity of respiratory distress for positive radiographs was therefore 58% but this was increased to 75% when only moderate or severe radiograph changes were considered. The specificity was 93% with either analysis. Among infants with no signs of respiratory distress, there was no difference in the mean length of hospital stay between those with positive radiograph and negative radiograph findings.

The prevalence of radiographic pneumonia in febrile infants under 3 months old, without signs of respiratory distress, was approximately 3% in this study. Only 1% of moderate or severe radiograph changes would have been unidentified by clinical signs. In this setting, however, the prevalence of radiographic pneumonia (6%) and moderate or severe radiograph changes (4%) was very low. As well, the infants in this study with moderate radiograph changes had benign clinical progression, which may not be the case in other settings. The authors suggested that chest radiographs be obtained in febrile infants under 3 months of age only when signs of respiratory distress are present.

King JC, Berman ED, Wright PF.
Evaluation of fever in infants less than 8 weeks old.
South Med J, 1987; 80(8): 948-952.

The purpose of this study was to evaluate the incidence of bacterial sepsis and meningitis as well as clinical or laboratory variables that could be used to predict which infants might not need hospitalization.

The records of 245 infants less than 8 weeks old, admitted with rectal temperatures of 38°C or higher, from the outpatient area of the University of Maryland Hospital, Baltimore, Maryland, USA, over a four-year period, were reviewed. An additional 97 consecutive infants admitted over a two-year period were prospectively evaluated. For these 97 infants, the paediatric resident recorded a general impression of sepsis (yes, no, unsure) after the history, physical examination, and initial laboratory results. All infants received a complete investigation for septicaemia.

Among all 342 infants, 13 (4%) had septicaemia and 9 (3%) had bacterial meningitis. Coagulase-negative staphylococci, isolated from 22 blood cultures, were excluded from this analysis. Pneumonia was found in 14 (4%) infants and bronchiolitis in 1 (0.3%). Among 97 infants evaluated prospectively, 61 were judged not to have a septic appearance. None of these infants had a positive blood or cerebrospinal fluid (CSF) culture, whereas 4 of 36 infants, judged by the resident to possibly have sepsis had positive cultures (2 CSF, 2 blood and CSF). The sensitivity, specificity, and positive predictive value of the judgement of septic appearance were 100%, 66%, and 11%, respectively, for bacteraemia or bacterial meningitis. The height of fever did not predict serious bacterial illness.

The authors concluded that, in their setting, clinical evaluation was the best indicator for the absence of serious bacterial disease.



00041982