

= Abstract =

Neonatal Sepsis and Antimicrobial Susceptibilities in the Neonatal Intensive Care Unit and Nursery

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Background : To delineate the changes in the causative agents of neonatal sepsis and their antimicrobial susceptibilities in the neonatal intensive care unit and nursery of Hanyang University Hospital during the past 10 years.

Methods : Hospital records of 15,144 patients hospitalized at the NICU and nursery of Hanyang University Hospital from 1989 to 1998 were reviewed and neonates diagnosed of neonatal sepsis were sorted and included in the study. The study period was divided into Period A(the first 5 years) and Period B(the second 5 years) to analyse causative agents and their antimicrobial susceptibilities.

Results : Neonatal sepsis was diagnosed in 170 patients(1.1%{Period A 1.2%, Period B 1.0%}) among the total of 15,144 inpatients. Two hundred isolates(Period A 109 isolates, Period B 91 isolates) were identified in 186 blood cultures(Period A 99 cultures, Period B 87 cultures) from 170 patients(Period A 91 patients, Period B 79 patients). The average age at the onset of the disease, when the initial blood culture was drawn, was 12.3 days old(Period A 8.8 days, Period B 16.3 days), and the proportion of the early onset disease was 34.7% in Period A and 23.0% in Period B, indicating that neonatal sepsis developed earlier during Period A. Among the isolated organisms including Gram positive bacteria[132(66.0%)], Gram negative bacteria [60(30.0%)], and fungi[8(4.0%)], coagulase negative Staphylococcus(CNS) was the most common organism(69/34.5%), followed by *Staphylococcus aureus*(36/18.0%), *Klebsiella pneumoniae*(17/8.5%), *Enterococcus*(12/6.0%), *Enterobacter cloacae*(8/4.0%), *Escherichia coli*(6/3.0%), and *Pseudomonas aeruginosae*(5/2.5%). The isolated fungi were *Candida parapsilosis*, *Candida albicans*, and *Trichosporon pullulans*. CNS, *S. aureus* and *Acinetobacter baumannii* were isolated more frequently in Period A compared to Period B. Antimicrobial susceptibilities of CNS and *S. aureus* to methicillin and the first generation cephalo-

sporins were decreased in Period B compare to Period A, those to aminoglycosides were increased in Period B, and vancomycin resistant strains were not identified. *K. pneumoniae*, Enterococcus, *E. coli*, and *P. aeruginosa* were isolated less frequently in Period B, compared to Period A. For *K. pneumoniae*, antimicrobial susceptibilities to the first generation cephalosporins were low in both Periods A and B, those to tobramycin and gentamicin were increased in Period B, and those to amikacin, ceftriaxone, and trimethoprim-sulfamethoxazole were high in both Periods A and B. Antimicrobial susceptibilities of Enterococcus to ampicillin, penicillin, and the first generation cephalosporins were decreased in Period B, but vancomycin resistant strains were not identified.

Conclusion : The occurrence rate of neonatal sepsis during the past 10 years in the NICU and nursery of the Hanyang University hospital was 1.1%, and the most common causitive agents were CNS and *S. aureus*, to which the antimicrobial susceptibilities to the first line drugs decreased in the later half of the study period with no vancomycin resistant isolates identified. Group B *Streptococcus* known to be the most common agent causing neonatal sepsis was not identified, and *K. pneumoniae* was isolated more commonly during the later half of the study period without decreased antimicrobial susceptibilities.

Key Words : Neonatal sepsis, Antimicrobial susceptibility, Neonatal intensive care unit

서 론

가 2).

10

가

48

72

1.

1989

1

1998

12

가

15,144

198

0.1~1%

가

1)

coagulase negative Staphylococcus, *Staphylococcus aureus* Group B streptococci

가

170

가

1).

2.

10
Period A, 1994

1989
1998

1993
Period B

1.

1.1%(170 /
15,144) , Period A 1.2%(91 /7,550),
Period B 1.0%(79 /7,594) .
186 200 7†
13 2 ,
11 2 , 2 3
, 1 1
National Com- 2
mittee for Clinical Laboratory Standards(NCCLS) 170
12.3 Period A 8.8 , Period B
16.3 Period B 7† Period A
3
54 (29.2%) , Period A 34
(34.7%), Period B 20 (23.0%) (Table 1).

Table 1. Demographic Data of 170 Neonates with Culture Proven Sepsis

	Period A(n=7,550)*	Period B(n=7,594)	Total(n=15,144)
No. of patients	91(1.2%)	79(1.0%)	170(1.1%)
No. of episodes	99(1.3%)	87(1.1%)	186(1.2%)
No. of organisms	109(1.4%)	91(1.2%)	200(1.3%)
Age at (+) blood culture (d)	8.8±12.6	16.3±24.8	12.3±19.6
No. of episodes of early onset(≤3d)	34/98(34.7%)	20/87(23.0%)	54/185(29.2%)
Birth weight(gm)	2,360.8±904.7	2,407.3±1008.5	2,383.0±952.9
No. of LBW(<2,500 gm)	49/87(56.3%)	40/79(50.6%)	89/166(53.6%)
IUP(W)	36.0±4.7	35.9±4.7	36.0±4.7
No. of premature baby(<37 w)	42/89(47.2%)	34/77(44.2%)	76/166(45.8%)
Infants with central lines	36/91(39.6%)	23/79(29.1%)	59/170(34.7%)
Infants on TPN	11/91(12.1%)	22/79(27.9%)	33/170(19.4%)
Infants with central lines and TPN	8/91(8.8%)	12/79(15.2%)	20/170(11.8%)
Infants with mixed infection	10/91(11.0%)	4/79(5.1%)	14/170(8.3%)
Infants deceased	19/91(20.9%)	5/79(6.3%)	24/170(14.1%)
With central lines and TPN	3/8(37.5%)	2/12(16.7%)	5/20(25%)
With mixed infection	3/10(30%)	0/4(0%)	3/14(21.4%)
Infants discharged AMA	11/91(12.1%)	9/79(11.4%)	20/170(11.8%)
With central lines and TPN	0/8(0%)	1/12(8.3%)	1/20(5%)
With mixed infection	1/10(10%)	1/4(25%)	2/14(14.3%)

*Total number of neonates admitted to the NICU and the nursery during the study period
LBW : low birth weight infants, IUP : Intrauterine period, TPN : Total parenteral nutrition

2. 가 166
 2,383.0 gm , Period A 2,360.8 gm, Peri-
 od B 2,407.3 gm . 2,500
 gm Period A 49
 (56.3%) 1,699.6 gm, Period B 40
 (50.6%) 1,529.3 gm . 가
 166 Intrauterine period(IUP)
 36.0 Period A 89 , 36.0 , Period B
 77 , 35.9 . IUP 37 76
 (45.8%) IUP 31.6 Period A
 42 (47.2%) IUP 31.8 Peri-
 od B 34 (44.2%) IUP 31.3
 (Table 1).

[100%(6/6)],
K. pneumoniae[83.3%(10/12)], *E. cloacae*[75%(6/8)]
A. baumannii[75%(3/4)] .

3. ,
 170 (Period A 91 , Period B 79
) 가
 59 (34.7%) Period A 36 (39.6
 %), Period B 23 (29.1%) ,
 33 (19.4%) , Pe-
 riod A 11 (12.1%), Period B 22 (27.9%) .
 가

20 (11.8%) , Period A 8 (8.8%), Period B
 12 (15.2%) . 가
 20 5 (25%) , Pe-
 riod A 3 (37.5%), Period B 2 (16.7%) ,
 . 14
 3 (21.4%) ,
 (Table 1).

170 (Period A 91 , Period B 79
) 27가
 14 (8.3%) , Period A 10 (11%),
 Period B 4 (5.1%) .

170 (Period A 91 , Period B 79
) 24 (14.1
 %) , Period A 19 (20.9%), Period B 5 (6.3%)
 ,
 20 (11.8%) , Period A 11 (12.1%),
 Period B 9 (11.4%) .

4.
 200
 (Period A 109 , Period B 91)
 132 (66.0%) 60 (30.0%),
 8 (4.0%) (Table 2).

coagulase negative Staphylococ-
 cus(CNS), *S. aureus*, Enterococcus가,
K. pneumoniae, *E. cloacae*, *E. coli*, *P. aeruginosa*
*A. baumannii*가
 , CNS가 69 (34.5%) 가
 , *S. aureus* 36 (18.0%),
K. pneumoniae 17 (8.5%), Enterococcus spp. 12
 (6.0%), *E. cloacae* 8 (4.0%), *E. coli* 6 (3.0%), *P.*
aeruginosa 5 (2.5%) .

CNS, *S. aureus*, *A. baumannii*
 Period A Period B 가 ,
 Enterococcus spp., *K. pneumoniae*, *E. coli*, *P. aeru-*
ginosa Period A Period B
 .
Candida parapsilosis, *Candida albicans*,
*Trichosporon pullulans*가 Period A
 2.8% Period B 5.5% Period B 가
 (Table 2).

가
 [100.0%(8/8)], *E. cloacae*[87.5%(7/8)], *K. pneu-*
moniae[64.7%(11/17)], *S. aureus*[44.4%(16/36)], CNS
 [21.7%(15/69)] .

5.
 가
 CNS, *S. aureus*, Enterococcus spp., *K. pneumoniae*,
E. cloacae, *E. coli*

Table 2. Microorganisms Isolated on Blood Cultures from Neonates with Sepsis

	Microorganism	Period A (n=109)	Period B (n=91)	Total (n=200)
Gram positive organisms	CNS	34(31.2%)	35(38.5%)	69(34.5%)
	<i>Staphylococcus aureus</i>	16(14.7%)	20(22.0%)	36(18.0%)
	Enterococcus	10(9.2%)	2(2.2%)	12(6.0%)
	<i>Streptococcus sanguis</i>	1(0.9%)	2(2.2%)	3(1.5%)
	β hemolytic streptococcus	1(0.9%)	2(2.2%)	3(1.5%)
	α hemolytic streptococcus	2(1.8%)	0(0.0%)	2(1.0%)
	Gram(+) bacilli	2(1.8%)	0(0.0%)	2(1.0%)
	<i>Streptococcus bovis</i>	0(0.0%)	2(2.2%)	2(1.0%)
	<i>Listeria monocytogenes</i>	1(0.9%)	0(0.0%)	1(0.5%)
	Streptococcus group F	1(0.9%)	0(0.0%)	1(0.5%)
	<i>Aerococcus viridans</i>	0(0.0%)	1(1.1%)	1(0.5%)
	Total	68(62.4%)	64(70.3%)	132(66.0%)
	Gram negative organisms	<i>Klebsiella pneumoniae</i>	15(13.8%)	2(2.2%)
<i>Enterobacter cloacae</i>		4(3.7%)	4(4.4%)	8(4.0%)
<i>Escherichia coli</i>		5(4.6%)	1(1.1%)	6(3.0%)
<i>Pseudomonas aeruginosa</i>		5(4.6%)	0(0.0%)	5(2.5%)
<i>Acinetobacter baumannii</i>		0(0.0%)	4(4.4%)	4(2.0%)
<i>Alcaligenes xylosoxidans</i>		2(1.8%)	0(0.0%)	2(1.0%)
<i>subspicis xylosoxidans</i>				
<i>Acinetobacter junii</i>		0(0.0%)	2(2.2%)	2(1.0%)
<i>Xanthomonas maltophilia</i>		0(0.0%)	2(2.2%)	2(1.0%)
<i>Pseudomonas picketti</i>		1(0.9%)	1(1.1%)	2(1.0%)
<i>Acinetobacter calcoaceticus</i>		1(0.9%)	1(1.1%)	2(1.0%)
<i>Aeromonas hydrophilia</i>		1(0.9%)	0(0.0%)	1(0.5%)
<i>Chryseobacterium meningosepticum</i>		1(0.9%)	0(0.0%)	1(0.5%)
<i>Klebsiella oxytoca</i>		1(0.9%)	0(0.0%)	1(0.5%)
<i>Pseudomonas</i> spp.		1(0.9%)	0(0.0%)	1(0.5%)
<i>Serratia marcescens</i>		1(0.9%)	0(0.0%)	1(0.5%)
<i>Costomonas testosteroni</i>		0(0.0%)	1(1.1%)	1(0.5%)
<i>Providencia alcalifaciens</i>		0(0.0%)	1(1.1%)	1(0.5%)
Salmonella group E		0(0.0%)	1(1.1%)	1(0.5%)
<i>Serratia fonticola</i>		0(0.0%)	1(1.1%)	1(0.5%)
<i>Veillonella</i> spp.		0(0.0%)	1(1.1%)	1(0.5%)
Total	38(34.9%)	22(24.2%)	60(30.0%)	
Fungus	<i>Candida parapsilosis</i>	1(0.9%)	3(3.3%)	4(2.0%)
	<i>Candida albicans</i>	2(1.8%)	1(1.1%)	3(1.5%)
	<i>Trichosporon pullulans</i>	0(0.0%)	1(1.1%)	1(0.5%)
	Total	3(2.8%)	5(5.5%)	8(4.0%)

CNS: ampicillin(Period A 3%, Period B 4.4%), methicillin(Period A 15.6%, Period B 9.1%), lincomycin(Period A 30%, Period B 50%), cefazolin(Period A 70%, Period B 50%), chloramphenicol(Period A 76.7%, Period B 84.6%), amikacin(Period A 69.7%, Period B 96.2%), vancomycin(Period A 100%, Period B 100%)

methicillin cefazolin Period B
chloramphenicol amikacin
Period B ,
vancomycin (Fig. 1).

S. aureus
methicillin(Period A 35.7%, Period B 9.1%), 1
cephalosporin(Period A 42.9%, Period B 7.1%), ka-
namycin(Period A 20%, Period B 0%), gentamicin
(Period A 46.7%, Period B 58.8%), amikacin(Period
A 86.7%, Period B 100%), chloramphenicol(Period
A 100%, Period B 100%), vancomycin(Period A
100%, Period B 100%) methicillin 1 cepha-
losporin, kanamycin Period A
Period B , gentamicin
amikacin Period B
chloramphenicol vancomycin 100%

(Fig. 2).
K. pneumoniae
1 cephalosporin(Period A 6.3%, Period B 0
%), gentamicin(Period A 21.4%, Period B 50%),
tobramycin(Period A 41.7%, Period B 100%), amika-
cin(Period A 93.3%, Period B 100%), ceftriaxone
(Period A 100%, Period B 100%), Trimethoprim-sul-
famethoxazole(TMP-SMZ)(Period A 100%, Period B
100%) 1 cephalosporin Period A, B
tobramycin gentamicin
Period B ami-

amikacin
chloramphenicol vancomycin 100%

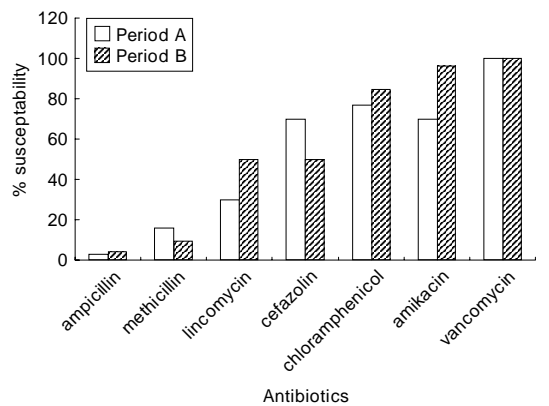


Fig. 1. Antibiotics susceptibility of coagulase negative staphylococcus(65 isolates).

kacin, ceftriaxone, TMP-SMZ Period A, B
(Fig. 3).

E. cloacae
ampicillin(Period A 33.3%, Period B 33.3%), carbe-
nicillin(Period A 50%, Period B 50%), gentamicin
(Period A 50%, Period B 75%), ceftriaxone(Period
A 100%, Period B 50%), TMP-SMZ(Period A 100
%, Period B 100%), chloramphenicol(Period A 75%,
Period B 100%) gentamicin Peiord B
ceftriaxone
Period B . Period A
B chloramphenicol TMP-SMZ
carbenicillin
(Fig. 4).

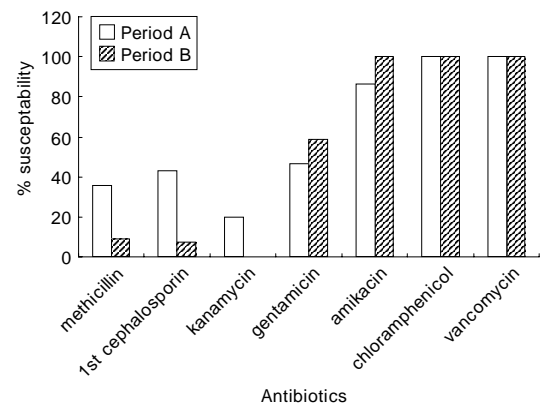


Fig. 2. Antibiotics susceptibility of Staphylococcus aureus(19 isolates).

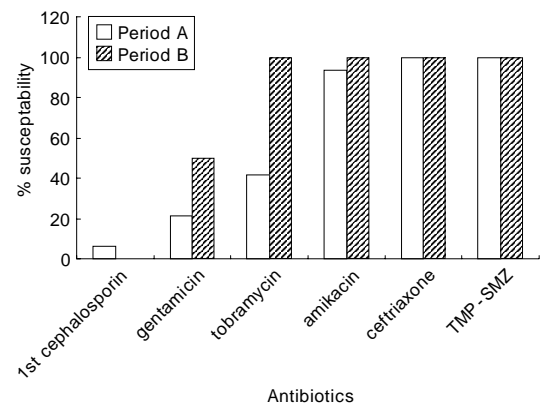


Fig. 3. Antibiotics susceptibility of Klebsiella pneumoniae(17 isolates).

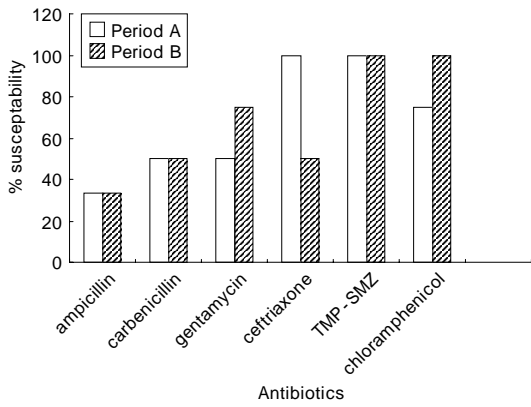


Fig. 4. Antibiotics susceptibility of *Enterobacter cloacae*(8 isolates).

E. coli Period B 16.7%
 Period A 10 가
 TMP-SMZ, kanamycin, amikacin
 ampicillin (16.7%)
 Enterococcus spp. Period B 2
 10 가 Period A
 , ampicillin, penicillin 1 cephalosporin
 vancomycin

0.1 ~ 1.0% 가
 1), 300 (30%) 가
 1,000 가
 7

(, , 7
 ,) ,
 , ,
 24 ~ 72
 3~7
 3
 .
 . 1950 *S. aureus*,
 1960 *E. coli*, *K. pneumoniae*, *Pseudomonas*
 , 1970
 group B Streptococcus(GBS), 1970
 methicillin-resistant *S. aureus*(MRSA)
 CNS가
 . 1990
 CNS Enterococcus,
 , *Candida*가
 2). 1996 CDC national noso-
 comial infection surveillance system(NNIS)
 CNS가(51%)
 가 GBS
 (7.9%), *S. aureus*(7.5%), *Candida*(6.9%), *E. coli*(4.3
 %), *Enterobacter*(2.9%), Streptococcus species
 (2.7%), *K. pneumoniae*(2.5%) . Jarvis
 WR 1987 1995 NICU
 (3)
 (4)
 group B Streptococcus가,
 CNS가 가
 , 1,000
 6.9 ~ 10.4 , 0.66~4.53%
 3-8), 1960 *E. coli* *S.*
aureus^{9, 10}, 1970 *S. aureus* ¹¹, 1980
*S. epidermidis*가 가
 5, 6, 12), 1997

CNS *S. aureus*가 가³⁾.
 10
 1.1% , 가
 CNS *S. aureus*, *K. pneumoniae*,
Enterococcus, *Enterobacter cloacae*, *E. coli*, *P. aeru-*
ginosae CNS *S. aureus* 가
 GBS가
 Back
 16, 17) *S. aureus* hexachlo-
 rophene
 Vancomycin MRSA
 vancomycin
 MRSA
S. aureus 76%
 64.3% 90.9% 가
 MRSA가 가
 CNS
 NICU
 50%²⁾ 1990
⁶⁾, ¹²⁾, ¹³⁾, ¹⁴⁾
K. pneumoniae
 CNS
 CNS¹⁸⁾
K. pneumoniae
 NICU *Staphylococcus hemolyticus*
Staphylococcus epidermidis 가 가
K. pneumoniae
¹⁵⁾ CNS 가
 가
 가
 penicillin, gentamicin SMZ, ceftriaxone
 vancomycin 가 *Enterococcus*
 penicillin, gentamicin *facium* *Enterococcus faecalis*
 vancomycin
¹⁹⁾
²⁾
 가 Staphylo-
 cocci (77%), (33%),
 가 가 40~90% (21%)
 Vancomycin

가²⁰⁾.
 12 *Enterococcus*
 3 가 . 10
 2
E. faecium *E. faecalis*
 1994 가
 2 *E. faecium*
 vancomycin resistant enterococcus(VRE)
Enterobacter *E. cloacae*가 가
 , 42~69% , Nagels²⁶⁾
²¹⁾ *Enterobacter* 80%
 , , , 37°C
 가 , ,
E. 6 *Acinetobacter*
*cloacae*가 4 , 4
 가 , 1
 가 , 1
²²⁾
Enterobacter 21 (18)가
 ampicillin ceftriaxone , gentamicin
 micin imipenem, ciprofloxacin
 , *Enterobacter*
 imipenem gentamicin
 micin . 1,500 gm
 19 ~ 47%
 8 gentamicin ceftriaxone 2.6 ~ 8.0% . *Candida*
 ampicillin , *Candida tropicalis*
 33.3% TMP-SMZ amikacin . *C.*
 cin 100% *albicans* . *C. pa-*
 rapasilosis
 가 가
E. coli 가
 40%가 K1 capsular antigen . *Candida* 15
 11 가 *C. albicans*
C. parapsilosis
 vaccine . 25~54% *C. albicans*
E. coli kanamycin, gentamicin amo-
 noglycosides TMP-SMZ , , ,

가^{27, 28)}
 가 2.8% 1989 1993 () 1994 1998
 5.5% 가 *C. parapsilosis*가 ()
 가 가 , ,
 8
 가 : 15,144 170
 , 가 1.1%(91 , 1.2%, 79
 1.0%) , 186 (99 , 87)
 200 (109 , 91)
 가 가 12.3
 8.8 , 16.3 ,
 34.7%, 23.0%
 , ampicillin cefotaxime 132
 3 cephalosporine ampicillin (66.0%), 60 (30.0%), 8 (4.0%)
 aminoglycoside 가 , Coagulase negative Staphylococcus(CNS)가
 , 가 69 (34.5%) 가 ,
¹⁾. *Staphylococcus aureus*(*S. aureus*) 36 (18.0%),
Klebsiella pneumoniae(*K. pneumoniae*) 17 (8.5%),
 Enterococcus 12 (6.0%), *Enterobacter cloacae*(*E. cloacae*) 8 (4.0%),
Escherichia coli(*E. coli*) 6 (3.0%), *Pseudomonas aeruginosa*(*P. aeruginosa*) 5 (2.5%)
 . *Candida parapsilosis*, *Candida albicans*, *Trichosporon pullulans*
 가 . CNS, *S. aureus* *Acinetobacter baumannii*(*A. baumannii*), *Candida*
 ampicillin gentamicin ,
 amikacin, vancomycin 3 cephalosporine , CNS *S. aureus* methicillin 1 cephalosporin
 가
 aminoglycosides 가
 , vancomycin .
K. pneumoniae, Enterococcus, *E. coli* *P. aeruginosa* *K. pneumoniae* 1 cephalosporin ,
 10 tobramycin gen-
 , tamicin 가 ami-
 kacin, ceftriaxone, trimethoprim-sulfamethoxazole
 . Enterococ-
 : 1989 1998 10 cous ampicillin, penicillin 1 cephalosporin
 vancomycin
 15,144

- 10
1.1% , CNS *S. aureus*가
vanco-
mycin
group B Streptococcus
, *K. pneumoniae*
- 1) Cole FS. Bacterial infections of newborn. In :
Tausch HW, Ballard RA, ed. Avery's Disease
of the Newborn. 7th ed. Philadelphia : WB
Saunders Co, 1998:490-512.
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the nursery. In : Remington JS, Klein JO, ed.
Infectious diseases of the fetus and newborn
infants. 5th ed. WB Saunders Co, 2001:1371-
418.
 - 3) , .
48
1998:53.
 - 4) , , , .
6
48
1998:378.
 - 5) , , , , ,
, , .
1987:30:130-7.
 - 6) , , , .
1990:33:1489-94.
 - 7) , , , .
1993:36:771-7.
 - 8) , , .
10
48
1998:53.
 - 9) , , , .
1966:9:
61-9.
 - 10) , , .
1968:11:229-35.
 - 11) , , , .
1975:18:567-75.
 - 12) , , , , .
1991:34:755-62.
 - 13) , , , , , .
1993:36:1542-53.
 - 14) , , , .
1994:37:1676-86.
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Enterobac-

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