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RISK FACTORS AND MICROBIOLOGY OF NOSOCOMIAL INFECTION AMONG NICU PATIENTS AT A TERTIARY HOSPITAL

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Abstract

A retrospective study was done on the risk factors and microbiology of nosocomial infection among NICU patients at the University of the East Ramon Magsaysay Memorial Medical Center. The study period was done from January 1, 1995 to August 31, 2000. Newborns were divided into 2 groups: those who developed and those who did not develop nosocomial infections. Based on the results, nosocomial infection was proven to be a significant cause of morbidity and mortality. The number of antibiotics used and duration of hospital stay are the risk factors found to be predictive of nosocomial infections. The predominant organisms isolated from all sites were mainly gram negative pathogens. Increased resistance of those organisms to aminoglycosides, cephalosporins, and extended spectrum penicillins was evident. The emergence of candidemia in the last two years of the study period was noted.

INTRODUCTION

Great strides in pharmacology and technology in the care of the newborn through the establishment of neonatal intensive care units made possible the survival of very small prematures. However, with this is noted a parallel increase in the incidence of hospital acquired infection. Although the number of hospital beds allotted to NICU is small, a large percentage of patients are infected with hospital acquired organisms. This translates to extended hospital stay, added hospitalization cost and eventually increased mortality rate.

It is the purpose of this paper to determine the incidence and risk factors associated with nosocomial infection in NICU together with the identification of etiologic agents and current management.

This knowledge will enable us to plan on surveillance of those with hospital acquired infection.

Keywords: Nosocomial infection, Neonatal intensive care unit
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MATERIALS AND METHOD

Medical records of all newborn admitted at the NICU of University of the East Ramon Magsaysay Memorial Medical Center, a tertiary teaching hospital from January 1995 to August 31, 2000 were reviewed.

Newborns were divided into 2 groups:

Those who developed and those who did not develop nosocomial infections

Factors such as the following were determined

Age of gestation, sex, weight, presence of fever, primary disease, procedure done, duration of stay, onset of nosocomial infection, number of antibiotic used and outcome.

Newborns with the following were excluded:

History of PROM, history of maternal infection, positive initial cultures and those admitted in other units for more than 48 hours or discharge from other units within 48 hours.

Culture and sensitivity results were likewise recorded.

Definition of terms

Nosocomial infection is defined as a localized or systemic condition that developed after admission to the hospital as an adverse reaction to the presence of an infectious agent or its toxins which is not present or incubating at the time of admission.

Nosocomial infections were considered ICU associated, if they developed in the ICU 48 hours after admission or within 48 hours of discharge from the unit, unless the clinical evidence strongly suggested otherwise.

Statistical analysis was done using the Chi square test, student's test and stepwise logistic regression to determine which among variables were significant as risk factors for nosocomial infection.

Table 1. Characteristics of 67 Patients with and without Nosocomial Infections and logistic Regresssion Analysis of Different Risk Factors

Patient Characteristics	NI(-)	NI(+)	Total	LR
Age				
<25 weeks	0	0	0	
26-28 weeks	3	5	8	
29-31 weeks	11	8	19	
32-34 weeks	9	7	16	
35-37 weeks	7	3	10	
≥38 weeks	7	7	14	
mean age:	33.03	32.73	t=0.35	
Standard deviation	3.24	3.63	p=0.728(NS)	
Sex:				
Male	21	15	36	
Female	16	15	31	
			x^2=0.304	
			p=0.581(NS)	
Weight				
500-1000 grams	8	3	11	
1001-1500 grams	7	12	19	
1501-2000 grams	8	8	16	
2001-2500 grams	7	1	8	
2501-3000 grams	5	2	7	
3001-3500 grams	2	3	5	
3501-4000 grams	0	1	1	
mean weight	1748.65	1711.67	t=0.19	
std. deviation	778.4	808.22	p=0.85(NS)	
SGA	14	10	24	
AGA	23	20	43	
LGA	0	0	0	
			x^2=0.1146	
			p=0.702(NS)	
No of antibiotics used				
0	4	1	5	3.2705
1	1	2	3	0.4029
2	18	2	20	7.1470
3	7	5	12	1.1317
4	4	5	9	0.6467
5	1	7	8	.1158
≥6	2	8	10	0.2022
mean	2.57	4.67	t=-4.13	
std. deviation	7.74	2.41	p=0.0000(sig)	
Duration of stay(days)				
0-3	19	3	22	5.14
4-7	5	4	9	1.0150
8-14	5	8	13	0.5056
15-21	3	3	6	0.81
22-28	2	5	7	0.3233
>28	3	7	10	0.3476
mean	11.51	24.73	t -2.92	
std. deviation	16.23	20.89	p 0.005(sig)	
Outcome				
Discharged improved	22	12	34	
Died	14	17	31	
Unknown(home per request, home against medical advice)	1	0	1	
Transferred	0	1	1	
chi square	2.508			
p			0.113(NS)	

between the two groups. Most of the subjects weigh less than two thousand grams with a mean weight of 1711.67 grams (NI+) and most were AGA (66.7%) (Table 1). Based on the primary disease (Table 2), 47.7% of patients from both groups had HMD, 22% had asphyxia neonatorum, and 12% had congenital anomalies (Cardiovascular, CNS, GIT). One patient

Table 2: Primary Disease Among Patients at NICU

With nosocomial infection	
- Hyaline Membrane Disease	14
- Asphyxia Neonatorum	9
- Twin to twin transfusion syndrome	1
- Congenital Heart Disease	2
- Congenital anomalies of CNS	1
- Congenital anomalies of GIT	1
Without nosocomial infection	
- Hyaline Membrane Disease	18
- Asphyxia Neonatorum	6
- Twin to twin transfusion syndrome	0
- Congenital Heart Disease	2
- Congenital anomalies of CNS	1
- Congenital anomalies of GIT	1

(1.5%) had twin-to-twin transfusion syndrome. The mean number of antibiotic used (Table 1) prior to onset of nosocomial infection was significantly higher in patients under NI(+) group with a mean of 4.67. Sixty-two percent (62%) of NI(-) patients were given <2 antibiotics wherein 66% of NI(−) patients received >4 antibiotics. The duration of hospital stay differ significantly between the two groups with the NI− group having a mean duration of 24.73 days compared to the NI- group with a mean duration of 11.51 days. Table 3 shows the most common procedures done during hospitalization, blood extraction (combined atrial

Table 3: Procedure done

Procedures done	NI(−)	NI(-)	LR
PD1			
Blood Extraction			
none	0	0	-
prick	0	0	-
venous	1	0	-
arterial	0	0	-
combination	36	30	0.973
PD2			
Intravascular access			
none	0	0	-
butterfly, needle	23	23	0.8109
cutdown, CVP	0	0	-
umbilical cath	0	0	-
combination	14	7	1.6223

Table 3: Procedure done *(continuation)*

Procedures done	NI(+)	NI(-)	LR
PD3			
Ventilatory support			
none	5	0	-
face mask	6	3	1.62
intubation	24	22	0.8854
tracheostomy	0	0	-
combination	5	5	0.8084
PD4			
Genitourinary tract intervention			
none	0	0	-
PUC	34	22	1.2537
catheterization	2	4	0.4060
combination	1	4	0.1341
PD5			
Central nervous intervention			
none	32	28	0.7341
lumbar tap	4	1	0.8182
ventricular tap	1	1	0.8120
tube ventriculostomy	0	0	-
combination	0	0	-
PD6			
surgical procedure			
none	28	30	1.3162
yes	9	10	0.5362
PD7			
GI access			
none	7	2	2.8208
yes	30	28	0.9335
PD8			
blood transfusion			
none	16	6	2.16
yes	21	24	0.71

and venous extraction 98.5%) intravenous access (usually IV cannula 68.7%), ventilatory support (maturity is intubation 68.7%), genitourinary tract intervention (maturity by use of pediatric urine collector 82.1%), central nervous intervention, GI access (mostly by oro-gastric tube 86.5%), surgical procedure 28.4%, blood transfusion 63.6%. The patient in the NI− mainly were placed on NPO, whereas of NI- patients were given enteral feeding (Table 4). Only 16.6% of NI(−) patients were placed on parenteral nutritional and 6.7% had combined IV and oral feeding.

Table 4: Type of Feeding

Type of feeding	NI(+)	NI(-)	LR
1. NPO	28	15	4.52269
2. Oral	2	10	0.1621
3. IV	5	7	0.5293
4. Combination	2	8	0.2023

Fifty-nine percent of NI(-) were discharged improved whereas only 40% of NI+ patients were sent home. One NI- patient was discharged per request and another patient belonging to the NI+ group was transferred to another hospital (Table 1). The onset of nosocomial infection ranged from 3 to more than 15 days after admission, with a mean duration of 7.80 days. Nosocomial infection usually occurred

Tabel 5: Onset of Nosocomial Infection

Number of days	Number of patients	Percent
3 days	3	10%
4-6 days	11	36.7%
7-9 days	8	33.3%
10-12 days	5	16.6%
13-15 days	2	6.6%
>15 days	1	3.3%
mean	7.80	
std. deviation	3.94	
Fever in Nosocomial Infection		
Hyperthermia	13	43%. (0.2528-0.6072)
Hypothermia	17	57% (0.3928-0.7472)
Normal	0	0%

95% Confidence interval

between 4 to 6 days (36.7%) after admission (Table 6). Among the NI+ patients fever occurred in 43% and 57% were mostly hypothermic. None of the patients had normal temperature (Table 6).

Table 6 Result of the Stepwise Logistic Regression Analysis

Risk factor	Coefficient weight	Standard error of coefficient	Relative risk
No. of antibiotics	0.657	0.185	1.929
Constant	-2.364		

α = 0.05
95% confidence level

Stepwise Logistic regression (BMDP) was used to determine which among the above variables were risk factors for the development of nosocomial infection. Among the variables tested, only the number of antibiotics used and duration of hospital stay were found to be significant. The relative risk of infection increases around 1.9 x for every 1 unit increase in the number of antibiotic received. With α = 0.05 or 95% confidence level, the number of antibiotic used can predict 74.6% of all cases correctly whether positive or negative.

Table 7: Nosocomial infection by site

Site	Number of patients	Percent
Respiratory tract	12	40
Bacteremia	15	50
GIT	3	10

The incidence of nosocomial infection was highest in the blood (50%), followed by the respiratory tract (40%), then GIT (10%) (Table 8). GIT infection was manifested as NEC. Regardless of the site, gram

Tabel 8: Pathogenic organisms

Organism	Number of organism	Percent
Acinetobacter	12	21.8
Candida non albican	4	7.2
Candida albican	3	5.4
Enterobacter aerogenes	2	3.6
Enterobacter cloacae	7	12.7
Enterobacter sp	3	5.4
Hafnia alvei	5	9.1
Klebsiella oxytoca	1	1.8
Klebsiella pneumoniae	4	7.2
Pseudomonas aeruginosa	2	3.6
Pseudomonas spp	1	1.8
Staphylococcus epidermidis	7	12.7
Staphylococcus aureus	1	1.8
Serratia rubidra	2	3.6
Serratia marcesceens	1	1.8

negative organisms predominate (Table 10). In the respiratory tract, the predominant pathogen belonged to the genus *Enterobacter* (35%) . There was only one isolate of *Staphylococcus epidermidis* (5.26%). On the other hand, *Acinetobacter* (22%) was predominant organism from the blood followed by *Candida spp.* Both albicans and non-albicans – 19.44%. *Enterobacter Cloacae* (16.66%) and *Staphylococcus epidermidis* (16.66%) ranked third. Majority of the *Candida sp.* were isolated for the pastlast years (1999-2000).

The antimicrobial sensitivity among gram negative organisms vary (figure 1-9). The sensitivity of *Enterobacter cloacae* to aminoglycosides vary. Highest resistance was seen for both Netilmycin (80%) and Tobramycin (100%) whereas Amikacin exhibited

Table 10: Etiologic Organisms according to site of nosocomial infection

Organism	Number of patients	Percent
Respiratory Tract		
Acinetobacter	4	21.05
Enterobacter aerogenes	2	10.52
Enterobacter cloacae	1	5.26
Enterobacter sp	3	15.79
Hafinia alvei	1	5.26
Klebsiella pneumoniae	3	15.79
Staphylococcus epidermidis	1	5.26
Serratia rubidra	1	5.26
Serratia marecseens	1	5.26
Pseudomonas aeruginosa	2	10.52
Bacteremia		
Acinetobacter	8	22.22
Enterobacter cloacae	6	16.66
Hafinia alvei	4	11.11
Klebsiella pneumoniae	1	2.7
Klebsiella oxytoca	1	2.7
Pseudomonas sp	1	2.7
Staphylococcus aureus	1	2.7
Staphylococcus epidermidis	6	16.66
Serratia rubidra	1	2.7
Candida non albican	4	11.11
Candida albican	3	8.33

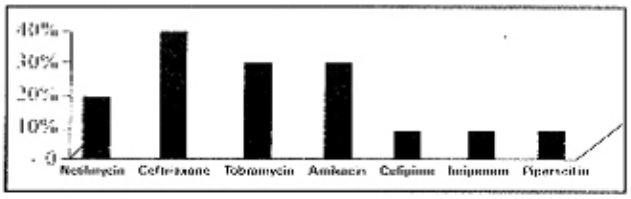

Fig. 1 Resistance Pattern of Acinetobacter

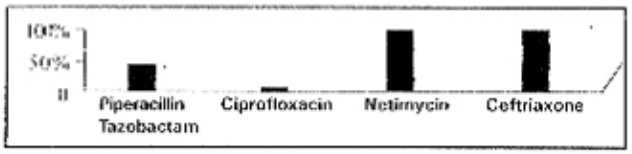

Fig. 2 Resistance Pattern of *Enterobacter spp*

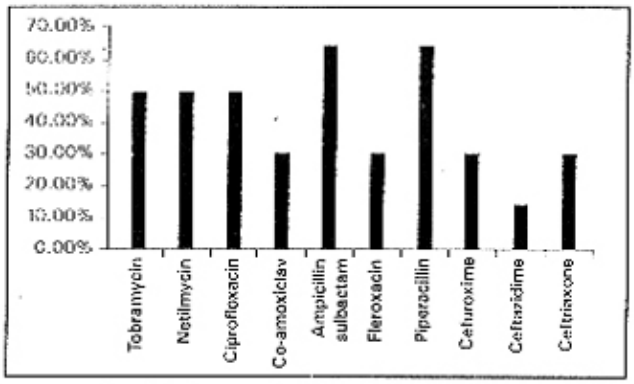

Fig. 3 Resistance Pattern of *Pseudomonas spp*

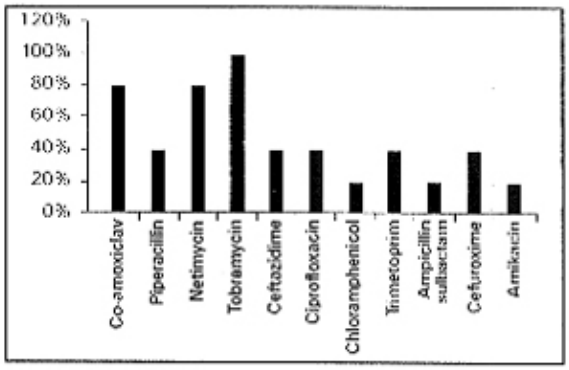

Fig. 4 Resistance Pattern of *Enterobacter cloacae*

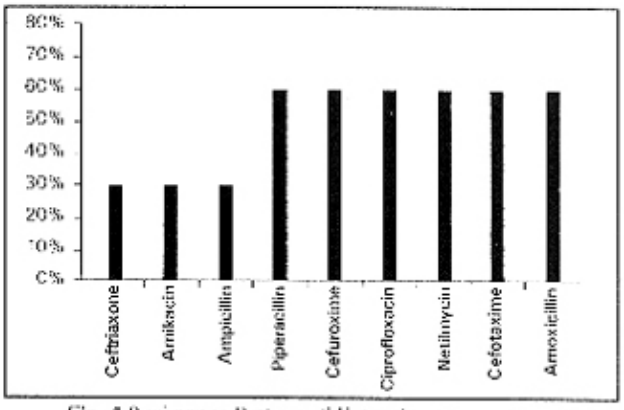

Fig. 5 Resistance Pattern of *Enterobacter aerogenes*

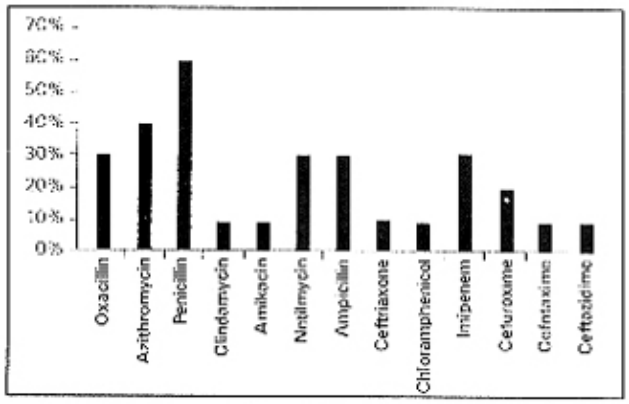

Fig. 6 Resistance Pattern of *Staphylococcus epidermidis*

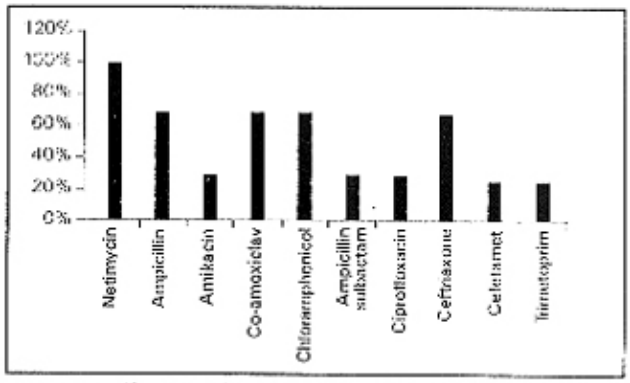

Fig. 7 Resistance Pattern of *Hafinia alvei*

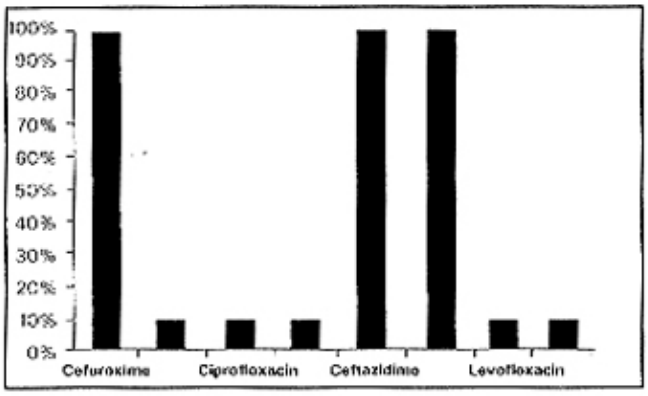

Fig. 8 Resistance Pattern of *Klebsiella oxytoca*

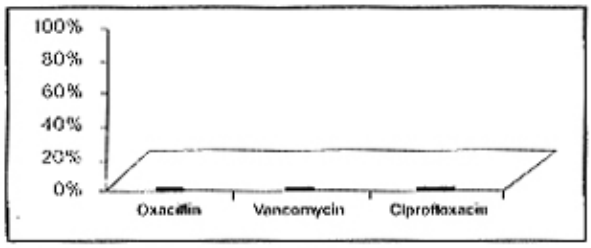

Fig. 9 Resistance Pattern of *Staphylococcus aureus*

the lowest resistance (20%). Forty percent resistance was likewise seen for the commonly used antibiotics, Ceftazidime and Piperacillin.

Pseudomonas aeruginosa showed 20% resistance to Ceftazidime. *Serratia marcescens* was resistant to all antibiotics tested. Acinetobacter showed 15-30% resistance to Aminoglycoside. Among the gram positive pathogens, *Staphylococcus epidermidis* showed 30% resistance to Oxacillin.

DISCUSSION

Nosocomial infections pose a serious threat to survival, particularly in pediatric patients whose immune system tend to be immature. It remains to be one of the leading causes of NICU related mortality. The 44.7% incidence of nosocomial infection reported in this study is considerably higher compared to 2-25% rate of NICU nosocomial infection reported in studies from United States.[1] Significant variation has been demonstrated among NICU's in morbidity and mortality. In one local study done, the prevalence of nosocomial infection range between 20-35% depending on the unit surveyed. The variation in reported rates probably occur because of the different definition of nosocomial infections clinical sepsis versus blood culture proven sepsis, different NICU settings and varying patient population. One of the major factors contributory to the rise of nosocomial infections is a break in the aseptic technique. Many hospital personnel fail to exercise basic infection control measures, particularly handwashing which is the simplest universal tool in the control of hospital acquired infection.

Nosocomial infection typically affect patients who are immunocompromised because of age-dependent, immune deficiency state, underlying diseases or medical/surgical intervention. It has been very well documented in literature that very low birth weight infants are prone to nosocomial infection. A study by Stoll et al on very low birth weight infants demonstrated that nosocomial infection in VLBW are in fact very common and carry significant mortality and morbidity. Several studies have emphasized the importance of host factors in the development of infection. Intrinsic or host factors such as age, sex, birth weight, did not significantly differ between the two groups in the study. Since the study involved NICU admissions, expectedly, patients were mostly prematures with low birth weight. Likewise, since most patients were prematures, hyaline membrane disease was most commonly associated underlying disease in both groups.

The role of various procedures such as intravascular catheterization, surgical intervention, parenteral nutrition in the occurrence of nosocomial infection were not reflected in the study. Likewise, the outcome between the two groups did not significantly differ. One limitation which can affect these results would be the small number of subjects included in the study.

Our analysis suggests that the distribution of the most common sites of infection is similar to that reported in other series,[2] where is blood stream infections ranked first followed by infections of the respiratory tract and GIT. Nosocomial respiratory tract infection is frequently associated with the use of any form of ventilatory support. Urinary tract infection which is most frequently reported in adult medical ICU's was not seen[2] in this study.

Among the variables studied, only two were found to be the risk factors predictive of nosocomial infection – the number of antibiotics used and duration of hospital stay. Nosocomial infection necessitating prolonged hospitalization has been implicated in the association between nosocomial infection and length of hospital stay. Prolonged hospitalization further exposes the patient to hospital

acquired pathogens and to various procedures and interventions.

The widespread and oftentimes injudicious use of antimicrobials is one of the major forces involved in nosocomial infections. Historically, the great increased concern about gram negative bacillary infection in the 1970's - 1980's led to increased use of cephalosporin antibiotics. Gram negative bacilli became resistant to these antimicrobials, as newer generations of cephalosporins and newer classes of antibiotics are being developed. By suppressing and altering normal bacterial flora, the use of multiple antibiotics predisposed patients to nosocomial infections.

The distribution of pathogens responsible for blood stream infection in the NICU reported in the US somewhat differs, wherein coagulase negative *staphylococcus* (CONS) represent 62% of isolates. Other predominant organisms include *Staph. aureus, Enterococci, Enterobacter* and *E. coli*. In our series, regardless of the site involved, gram negative pathogens predominate.

Increased resistance to aminoglycosides, cephalosporins, and the extended spectrum penicillins was clearly evident in our study. Worldwide, acquired antimicrobial resistance is a growing problem. Vancomycin-resistant *S. aureus* is the pathogen of greatest concern. *P. aerugenosa, Klebsiella* and *Enterobacter* that harbor chromosomal or plasmid mediated betalactamase enzyme are the major resistant gram negative pathogens.

While bacterial resistance increases as a major threat, the emergence of fungal infection is becoming a growing concern. This is reflective by the emergence of *Candida sp.* bacteremia during the last two years of the study period. The incidence of *Candida* infection is increasing in university and tertiary care hospitals. Candidemia was provoked by the use of many broad spectrum antibiotics and prolonged hospital stay. Prolonged exposure to antimicrobials, parenteral nutrition, tracheal intubation, umbilical artery catherization and low gestational age have been reported to increase the frequency of Candidal infections in premature infants.[12]

CONCLUSION

Incidence of nosocomial infection in this NICU still remains to be high at 44.7%. Risk factors determined in the study were number of antibiotics used and duration of stay in the hospital. In the NICU setting, patients with prolonged hospital stay should be treated using aseptic technique such as hand washing, wearing gown and mask, and adherence to the guidelines recommended by the infection control committee. The most common organism in the NICU setting is usually gram negative bacteria such as Acinetobacter which is sensitive to piperacillin-tazobactam and cefepime.

RECOMMENDATION

To make a similar study involving multicenters for a bigger sample size.

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