Carriage of Community-Associated Methicillin-Resistant
Staphylococcus aureus in a Cohort of Infants in Southern
Israel: Risk Factors and Molecular Features

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Abstract

There are few data about the epidemiology of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) in children in Israel. This study was intended to identify risk factors for CA-MRSA colonization in healthy infants, to characterize the molecular features of colonizing organisms and to determine whether they are responsible for healthcare-associated (HA) infections. Nasal cultures and demographic details were collected from a cohort of healthy infants at 5 visits between 2 and 12 months of age. Clinical characteristics of pediatric methicillin-resistant *Staphylococcus aureus* (MRSA) blood-stream infections (2001 to 2006) and wound cultures collected over 6 months were studied. Clonal structure was evaluated with multilocus sequence typing. Isolates were studied for staphylococcal cassette chromosome *mec* (SCC*mec*) type, and for the presence of *pvl* genes. MRSA was cultured at least once from 45 of 659 infants (Jewish-346, Bedouin-313). 40/45 (89%) were from Bedouin infants. 29/45 (64.4%) belonged to a new clonal complex designated CC-913, that carries SCC*mec* IV but not the *pvl* genes. CC-913 was also isolated from 9/14 blood cultures and 7/8 wounds. All CC-913 infections occurred in Bedouin children and all but two were HA.

In conclusion, Bedouin origin was the main risk factor for carriage of CA-MRSA. CC-913 was dominant both in healthy carriers and as a cause for pediatric healthcare-associated MRSA blood-stream infections.
Introduction

Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has become a worldwide problem, although its prevalence varies considerably among countries. Consistently high prevalence is found in the USA, South America, Japan and southern Europe, whereas prevalence is low in Scandinavia, The Netherlands and Switzerland (9, 19, 21-22, 44).

Clusters and outbreaks of CA-MRSA infections have been described in ‘closed populations’, such as Native Americans (16), prison inmates (4), children attending childcare centers (1), military recruits (50), and competitive sports participants (4). Moreover, CA-MRSA, originally found mainly in the community has now been introduced into the hospital setting (19, 28, 35). At some hospitals, CA-MRSA strains are even displacing classic hospital-acquired strains of methicillin-resistant *Staphylococcus aureus* (MRSA) (45).

There are few reports of CA-MRSA in Israel. A recent study reported low prevalence of MRSA carriage (0.11%) in children attending outpatient clinics in central Israel (33). One of the earliest descriptions in the world literature of a CA-MRSA outbreak occurred in 1997 in 20 patients in a facility for adults with developmental disabilities in southern Israel (3). Isolates from all the outbreaks had a single *Sma*I macrorestriction pattern, but other molecular characteristics were not sought.
The IsraPrev study is an ongoing investigation, initiated in August 2005, designed to evaluate the effect of different scheduling protocols of a 7-valent pneumococcal conjugate vaccine (PCV7) on carriage of *Streptococcus pneumoniae* and *S. aureus* in healthy infants. During this study, a surprisingly high prevalence of MRSA carriage (up to 4.4% of all children) was noted, almost exclusively among Bedouin infants.

Our objectives were to investigate: 1) the clonal structure and the molecular characteristics of MRSA isolated from healthy infants from southern Israel; 2) whether CA-MRSA has penetrated the hospital environment and to characterize the clinical features of CA-MRSA infections; 3) the relationship between CA-MRSA strains in southern Israel and previously characterized clones (Israeli and global); and 4) the risk factors for MRSA carriage in healthy infants in southern Israel.
Materials and Methods

Setting

In southern Israel (the Negev region), Jewish and Bedouin populations differing in their socioeconomic conditions and lifestyles live side by side. However, both have access to the same medical services. The Jewish population is mainly urban, whereas the Bedouin population is in transition from a nomadic existence in the desert to a western lifestyle (38). Contact between children of the two populations is rare. The Bedouin population is characterized by overcrowding, lower education level, larger family size and lower income than the Jewish population (38). In 2004, the crude birth-rate was 55.3 vs 21.0 per 1000 in the Bedouin and Jewish populations (39) respectively and the mean family size (±SD) in the Bedouin population was 8.2±0.9 persons vs only 3.2±0.1 in the Jewish population (40). The average monthly family income was two-fold higher in the Jewish population (39). Hospitalization rates for respiratory and other infectious diseases were higher among Bedouin than among Jewish children (23).

All children in the area are born in one hospital, where they also receive all emergency and inpatient services. Over 60% of children in the Negev region are medically insured in the largest health plan in Israel, the General Health Insurance Plan.
Patients

*IsraPrev study* - MRSA carriage and molecular characterization of MRSA strains were determined in infants participating in the IsraPrev study, as described in the introduction. Healthy 2-month old infants were enrolled and evaluated at 5 visits (age 2, 4, 6, 7 and 12 months). At each visit, demographic data (age, gender, number of children) and medical history (antibiotic use, previous illness such as acute otitis media (AOM), asthma, etc.) were gathered and anterior nares swabs were collected for *S. aureus* isolation. The study protocol was approved by the ethics committee of the Soroka University Medical Center.

Clinical cases: - All cases of pediatric (<18 years) MRSA blood-stream infection from 2001 to 2006 were included. All children that had MRSA isolated from wound cultures during a 6-month period in 2006 were included. Health care–associated MRSA cases were defined as patients with (1) an MRSA infection identified after 48 hours of admission to a hospital; (2) a history of hospitalization, surgery, dialysis, or residence in a long-term care facility within 1 year prior to the MRSA culture date; (3) a permanent indwelling catheter or percutaneous medical device (eg, tracheostomy tube, gastrostomy tube, or Foley catheter) present at the time of culture; or (4) a known positive culture for MRSA prior to the study period (25).
Outbreak strains: Isolates of MRSA collected during an outbreak of skin infections that occurred in 1997 in an institution for adults with mental disability (3) were studied for their molecular characteristics.

Microbiologic methods

Antimicrobial susceptibility testing was performed by disk-diffusion assay. Resistance to methicillin in *S. aureus* was tested by cefoxitin disk-diffusion method and confirmed by agglutination test for the production of PBP2a (Oxoid LTD, Cambridge, UK). Screening for Vancomycin-Intermediate/Resistant *Staphylococcus aureus* was performed by the agar screening plate method, according to CLSI recommendations (6).

Pulsed-Field Gel Electrophoresis (PFGE): Determination of Smal macrorestriction patterns was performed as previously described (14). In short, cell suspension was mixed 1:1 with 1.2% agar (SeaKem Gold agarose, Lonza, ME, USA) and poured into wells. Agar plugs were lysed in a shaker incubator, first with lysozyme (1mg/ml) for 4 hours in 37 °C, and then in proteinase K (1 mg/ml) for 4 hours in 50 °C. Plugs were washed 6 times in TE solution. Plugs were cut and digested for 2 hours with 30 U of *Smal* enzyme. The plugs were then inserted into PFGE gels (1% SeaKem Gold agarose) and gels were run on a CHEF Mapper XA® (BioRad, Hercules, CA, Cat. 170-3672). The PFGE pulse ramp was 5-15 seconds for the first 10 hours, and then 15-60 seconds for the last 13 hours. The voltage was 6 V/cm and the angle was 120°. Gels stained with ethidium bromide were photographed with a ChemiDoc XRS®.
camera (BioRad, Hercules, CA, Cat. 170-8070) and were analyzed with a
Fingerprinting II Software version 3.0 (BioRad, Hercules, CA). Isolates were
considered related if the macrorestriction patterns had ≤6 bands difference, according
to the Tenover criteria (43).

**Multilocus Sequence Typing (MLST):** MLST was performed on representative strains
from each PFGE cluster and sub-cluster, according to a standardized protocol (12).
MLST results were analyzed by the eBURSTv3 software (http://www.mlst.net).

**Staphylococcal Cassette Chromosome mec (SCCmec) typing:** SCCmec typing was
determined by multiplex PCR (49). PCR reaction was done with a PCR Master Mix
(Promega, Madison, WI) with a Biometra TGradient Thermo Cycler apparatus
(Biomedizinische Analytik, Göttingen, GmbH). Ambiguous results were also tested by
single target PCR for the ccr and the mec complexes (49).

**Determination of agr type and the presence of the pvl and the arcA genes:** agr typing
was performed by multiplex PCR (25). The presence of the lukS-PV and lukF-PV
genes (24) and the arcA gene (10) was tested by PCR. These genes were sought as
they are present in many CA-MRSA strains around the world (pvl) (11, 24, 26, 30) or
in the USA300 strain (arcA) (10) and may play a role in the virulence of CA-MRSA
infections.
Data analysis and statistical methods

Molecular characteristics were studied in all patient-unique MRSA isolates detected in the IsraPrev study, the clinical cases and the outbreak isolates. Risk factors for MRSA carriage were studied only in infants who had attended all first 5 visits of the IsraPrev study. Variables included in the analysis were 1) demographic: age, gender, ethnicity, type of residency for Bedouin children; 2) socioeconomic: number of siblings, number of people in child’s room, smoking in the infant’s home, breast-feeding; and 3) health-care related: antibiotic use since last visit and previous hospitalization.

To detect differential risk factors for MRSA carriage, comparisons were done as follows- MRSA vs. MSSA and S. aureus (total) vs. non-carriers. No distinction was made between transient vs. persistent carriers.

Continuous variables were assessed using the t-test, and categorical variables with $\chi^2$ or Fisher-exact tests, as appropriate. In multivariate analysis, performed for S. aureus (total) vs. non-carriers, risk factors found to be related to the dependent categorical variable at $p \leq 0.1$ were entered into logistic regression models.

Survival analyses were done using the Kaplan-Meier method. For all analyses, $\alpha$ was set as 0.05. All analyses were performed using the Statistical Package for the Social Sciences (SPSS for Windows, version 14.0, SPSS, Inc.).
Results

A total of 659 infants (Jewish-346, Bedouin-313) were recruited from September 2005 to June 2006. Of those, 553 infants participated in all first 5 visits and were thus included in the risk factor analysis. Of the 553 infants participating in the risk factor analysis, MRSA was isolated from nasal cultures at least in one visit from 32 infants (5.7%) and MSSA from 268 (48%). Of the 32 carriers, MRSA was isolated once in 24 infants, twice in 3 infants and 3 times in 5 infants.

Risk factors for MRSA carriage

The age-specific prevalence of S. aureus carriage in Jewish and Bedouin children is presented in figure 1. The prevalence of MSSA carriage decreased from 167/553 (30%) at 2 months to 55/553 (10%) at 12 months and was not significantly different between Jewish and Bedouin infants. A single exception was an increase in the prevalence of MSSA carriage (65/301 to 69/301) that was observed in Jewish infants at 4 and 6 month of age, respectively. However the prevalence of MRSA carriage differed significantly between the populations: carriage in Bedouin infants was 11/252 (4.4%) and 6/252 (2.4%) at age 2 and 12 months, respectively. In contrast, among Jewish infants, carriage did not exceed 0.66%. New acquisition curves (cumulative) for MSSA and MRSA carriage according to ethnic origin are presented in figures 2-3, respectively. The risk for new acquisition of MRSA was significantly higher in Bedouin than in Jewish children (RR= 6.62, 95% CI= 2.55-17.2, p<0.001). Seven
Bedouin infants carried both MRSA and MSSA at some point of time. Among the 5 Jewish infants that carried MRSA, 3 also carried MSSA.

To avoid bias associated with ethnicity, since only 5 Jewish children carried MRSA, further analyses were performed only in Bedouin infants (MRSA n= 20, MSSA n= 110, no S. aureus n= 115). No risk factor was associated with MRSA carriage compared to carriage of MSSA (the 7 infants with dual isolation of MSSA and MRSA were excluded from this analysis). The following risk factors were associated with carriage of S. aureus (MSSA and MRSA combined): Previous use of antibiotics (16.8% vs. 6.1%, p=0.009) and past hospitalization (13.1% vs. 3.5%, p=0.007) for S. aureus carriers vs. non-carriers, respectively. In multivariate analysis, the only independent variable in which a significant difference was found between carriers vs. non-carriers was past hospitalization (RR= 4.2, 95% C.I.= 1.38-12.79, P=0.012 for S. aureus carriers).

Bacteriologic and molecular features of MRSA strains

The cluster analysis of SmaI macrorestriction pattern of MRSA isolates from healthy infant carriers (n=45) is presented in figure 4. Three clusters were identified: cluster A was the most common (28/45, 62%), followed by cluster B (9/45, 20%) which included 3/5 Jewish children with MRSA carriage, all of whom attended the same Maternal and Child Health centers.
The clonal structure of MRSA isolates from healthy infant carriers is presented in Figure 5. PFGE cluster A is a new Clonal Complex (CC) CC913, structured from 3 new Sequence Types (ST), including one from a non-related PFGE type (ST914). The second most common PFGE cluster B was identified as the new ST915. Two additional new STs were identified – ST 911 and ST916.

The clinical MRSA isolates included 14 blood culture isolates and 8 wound culture isolates. One wound culture isolate was from patient no. 7 who also had bacteremia.

Sixteen out of the 22 clinical isolates (72%) belonged to cluster A (CC913) (PFGE data not shown). The other 6 isolates were: ST915 (from cluster B, n=1), ST80 (n=3), ST5 (n=1) and ST228 (n=1) (Figure 5). All the main clones in the study (CC913, ST915, ST45 and ST80) carried SCC mec type IV (Figure 5). The only clone that carried the pvl genes was ST80, and arcA was not found in any of the isolates.

Resistance to antimicrobial agents other than β-lactams was as follows: Trimethoprim-sulphamethoxazole-2/22, gentamicin-3/22, clindamycin-9/22, erythromycin-9/22 and ciprofloxacin-3/22. Vancomycin-intermediate strains were not found.

Clinical and epidemiological features of pediatric MRSA infections

The clinical and demographic characteristics of pediatric MRSA infections are presented in Table 1. ST80 infections included necrotizing pneumonia, mastitis and necrotizing soft tissue and bone infection. The last two occurred in previously healthy children without risk factors for health-care related infections, both of them from the...
Bedouin township of Hura. Of note, children from this township were not part of the carriage study.

In contrast, 13/15 of CC913 infections were in children with various significant underlying diseases and the acquisition was health-care associated. Of note, 4 of these children had congenital insensitivity to pain with anhydrosis (CIPA), an inherited disorder that is relatively common among Bedouin children. These children presented with osteomyelitis or with stump infections. Only 2 cases (patients 10 and 15) were community-acquired and occurred in previously healthy children. One 3.5-year old child with hyper-IgE syndrome and chronic lung diseases had persistent CC913 bacteremia and subsequently died of *Pseudomonas aeruginosa* sepsis. The other MRSA infections (caused by ST5, ST228 and ST915) were hospital-acquired bloodstream infections (BSIs) in children with various underlying diseases.

Relationships between isolates from this study, the 1997 outbreak and global clones Five MRSA isolates from skin infection and 4 isolates from carriers were studied during the 1997 outbreak (3). All isolates had an identical *SmaI* macrorestriction pattern (data not shown) and were identified as ST30. Although ST30 was also identified in one carrier in the present cohort study, the strains differed by the SCCmec sub-type (IVa vs. IVc) and by the presence of *pvl* genes in the outbreak strain but not in the carrier strain.

Although most STs in the study, including the new ST915, were related to known clonal complexes, CC913 was not (data not shown).
Discussion

We found that the prevalence of MRSA nasal carriage in healthy infants in southern Israel was significantly higher in Bedouin than in Jewish infants. The prevalence of overall *S. aureus* carriage was comparable between the ethnic groups and decreased during the first year of life, as described by others (17, 31). The prevalence of MRSA carriage in Jewish infants in our study during the first year of life ranged between 0 to 0.66%. Previous studies reported lower prevalences of MRSA (0.15%-0.11%) in children attending outpatient clinic in Jerusalem (36) and central Israel (33), respectively. Molecular features were studied only in the latter study (33) and only 2 of the 5 MRSA isolates (3 were isolated from adults) harbored SCC\textit{mec} type IV and were identified as ST45, as was found in 3 infants in our study. On the other hand, the prevalence among Bedouin infants ranged from 4.4% to 2.4% at 2 and 12 months, respectively. By comparison, this prevalence is comparable to the prevalences of 0.6% and 2.2% that have been reported from Chicago (18, 42), an area with high rate of CA-MRSA infections, and lower than the 9.2% prevalence reported from Nashville (7).

Increased rates of CA-MRSA infections among semi-closed minority populations have been reported from different parts of the world, including Native Americans in the USA (15, 41) and Canada (29) and the indigenous population in Australia (47). In the Canadian (29) and the Australian (47) studies, CA-MRSA isolates were polyclonal, whereas in the two studies from the USA (16, 41), the majority of isolates
belonged to PFGE type USA400, suggesting dissemination from a common precursor. USA400 is also a common CA-MRSA clone in the general population in the USA. In contrast, we have found that most of CA-MRSA isolates found in Bedouin infants belonged to a single clone designated CC913 that was not related to any known MLST clone and was isolated almost exclusively from Bedouin infants. In the Canadian study (29) it was hypothesized that the high rate of CA-MRSA infections in minority populations is related to conditions associated with poverty, such as overcrowding and high hospitalization rate. These conditions are also prevalent in the Bedouin population (data not shown). However, the overall prevalence of S. aureus carriage was not higher among Bedouin children than among Jewish children. Since Bedouin children live in crowded conditions and separately from the Jewish children, it is not surprising that one single clone (CC913) was disseminated in this population and was not prominent in Jewish children.

Prior hospitalization was the only independent risk factor for overall S. aureus carriage found in our analysis. Although the association between hospitalization (15), various chronic diseases, such as diabetes, renal failure and cirrhosis (48) and high rate of S. aureus carriage is well known, the association with hospitalization has not been reported previously in infants without such conditions. This suggests the importance of nosocomial cross-transmission of S. aureus even in infants and young children.

Clonal complex 913 was responsible for the majority (9/14) of pediatric MRSA bloodstream infections and was the most common isolate (7/8) from wound cultures.
Although our data are limited due to the relatively short duration of wound culture sampling and the lack of cultures from other sites of MRSA infection, they indicate that CC913 may now have become the main cause for pediatric MRSA infections at the Soroka University Medical Center. Surprisingly, most cases (13/15) were healthcare related and occurred in children with underlying diseases. In the USA and France, CA-MRSA and hospital-acquired (HA)-MRSA clones were thought to be distinct from each other (46). The USA CA-MRSA differed from HA-MRSA by the presence of \( pvl \) genes, \( SCCmeC \) type IV, \( agr \) type III and their relative susceptibility to non-\( \beta \)-lactam antimicrobials. In recent years, there have been numerous reports, including from Israel (32), describing nosocomial outbreaks caused by strains harboring \( SCCmeC \) type IV. In the USA, the USA300 pulsotype has penetrated into hospitals and is now a common cause for HA-MRSA infections in some institutions (37). In other countries (2, 5, 8, 30, 34, 46), strains harboring \( SCCmeC \) type IV have been identified as major causes of HA-MRSA infections. Studying Japanese hospitals, Ma et al (26) have demonstrated a transition in the common MRSA clones isolated from 1979-1985 to the 1990s, from ST30, \( SCCmeC \) type IV, \( pvl \) positive strain to ST5, \( SCCmeC \) type II strain, respectively. Therefore, considering that the dominant strains in our study, CC913 and ST915, (all harboring \( SCCmeC \) type IV) were isolated from healthy carriers and community-acquired infections but also from hospital-acquired infections, it is impossible to conclude whether these strains originated in or outside the hospital environment.

The clinical spectrum of CC913 infections from our collection included mainly catheter-related blood stream infections, osteomyelitis and wound infections,
resembling the spectrum of HA-MRSA infections (20, 27). On the other hand, the two
*pvl*-carrying strains found in our study, ST80 and the ST30 outbreak strain (3) were
characterized by severe life-threatening infections (ST80) and an outbreak of skin
infections (ST30) resembling the clinical spectrum observed in CA-MRSA infections
from France and the USA (10, 11, 13, 27). Whether the difference in the clinical
spectrum between CC913 and ST80 infections is explained by the lack and presence
of the *pvl* genes, respectively, goes beyond the scope of this study.

The main limitation of our study is the paucity of clinical isolates of MRSA from
sources other than blood cultures, as discussed above and the lack of clinical isolates
collected in the outpatient setting. Thus, we lack data about the molecular
epidemiology of the more common, less complicated community-acquired
staphylococcal skin infections. Another limitation is the lack of data on exposure to
possible sources of *S. aureus*, such as the presence of skin infections or occupation in
a health-care facility of a family member, since this study was not initially designed to
explore this question.

In conclusion, we found that a new SCC*mecc* type IV MRSA clone, designated
CC913, was the cause of most pediatric MRSA BSIs at the Soroka Hospital, as well as
the relatively high MRSA carriage prevalence among healthy Bedouin infants.
Although this clone does not seem to cause severe community-acquired infections,
such as necrotizing pneumonia and soft tissue infections, its dissemination among
Bedouin children may have adverse implications for therapeutic options. Further
studies are required to better describe the epidemiology of community-acquired
infections, to track the origin of CC913 and to describe its unique genetic characteristics.
Figure legends

Figure 1. Prevalence of *S. aureus* carriage in Jewish (1a, n=301) and Bedouin infants (1b, n=252).

Figure 2. New acquisition curve (cumulative) of MSSA (2a, p=0.18 for ethnicity). carriage in Jewish and Bedouin infants.

Figure 3. New acquisition curve (cumulative) of MRSA (RR for Bedouin infants= 6.62, 95% CI= 2.55-17.2, p<0.001) carriage in Jewish and Bedouin infants.

Figure 4. Cluster analysis of *Smal* macrorestriction pattern of MRSA isolates from healthy infant carriers (n=45). B- Bedouin; J- Jewish.

Figure 5. Clonal structure, SCC*mec* and *agr* typing of MRSA isolates from 45 carriers (ca) and 22 clinical isolates (cl). Bold capital letters indicate the corresponding PFGE patterns (figure 3). Black lines indicate single locus variation and gray lines indicate double locus variation.
References


of isolates collected in the United States, Canada, Latin America, Europe, and the
Western Pacific region for the SENTRY Antimicrobial Surveillance Program,

10. Diep BA, Gill SR, Chang RF, Phan TH, Chen JH, Davidson MG, Lin F, Lin
J, Carleton HA, Mongodin EF, Sensabaugh GF, Perdreau-Remington F.

infections in France: emergence of a single clone that produces Panton-Valentine

sequence typing for characterization of meticillin-resistant and meticillin-

13. Fridkin SK, Hagement JC, Morrison M, Sanza LT, Como-Sabetti K,
Jernigan JA, Harriman K, Harrison LH, Lynfield R, Farley MM; Active
Bacterial Core Surveillance Program of the Emerging Infections Program


staphylococci; influence of hospitalization on carrier rate in patients, and their

KA, Cheek JE. 2001. Community acquired meticillin-resistant Staphylococcus
aureus in a rural American Indian community. JAMA. 286: 1201–1205.

nasopharyngeal bacterial flora in infancy: effects of age, gender, season, viral


24


43. Tenover FC, Arbeit RD, Goering RV, Mickelsen PA, Murray BE, Persing DH, Swaminathan B. 1995. Interpreting chromosomal DNA restriction patterns


Figure 4.
Table 1. Demographic and clinical characteristics of pediatric MRSA infections. ST-sequence type; m-months; w-weeks; B-Bedouin; J-Jewish; TPN- total parenteral nutrition; CIPA- congenital insensitivity to pain with anhidrosis; HA-healthcare associated; CA- Community associated; CVC- central venous catheter; BSI- blood stream infection.

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<th>Patient number</th>
<th>ST</th>
<th>Age (y)</th>
<th>Sex</th>
<th>Ethnicity</th>
<th>Year</th>
<th>Underlying Conditions</th>
<th>Isolation site</th>
<th>Acquisition</th>
<th>Clinical diagnosis</th>
<th>Complications</th>
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<td>913</td>
<td>3 m</td>
<td>M</td>
<td>B</td>
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<td>Blood</td>
<td>HA</td>
<td>CVC-BSI</td>
<td>Metastatic infection (bone)</td>
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<td>F</td>
<td>B</td>
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<td>B</td>
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