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Hickman catheters in association with intensive cancer chemotherapy

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Abstract. Hickman catheters were the major venous access devices utilized at the University of Maryland Cancer Center from November 1978 to 1987. This study provided an opportunity to standardize insertion technique, to manage catheter-related activities and daily maintenance procedures in order to examine the progression of Hickman-catheter-related problems, to identify those factors that may minimize them, and to develop guidelines for the management and prevention of complications and malfunctions. In all, 690 Hickman catheters (368 double lumens) were placed in patients with acute leukemia and other cancers: 401 catheters were placed in patients with leukemia; 269 were placed during neutropenia; and 230 at platelet counts of $<50000/\mu l$. Two surgeons inserted 490 catheters, and the remaining 200 were placed by a group of rotating surgeons. All catheters were placed with the intention that they would remain in place as long as clinically necessary. Total Hickman catheter days were 134273. Infectious complications included exit site infections (160), tunnel infections (46) and bacteremias (397). There were 438 instances of noninfectious complications including thrombosis, lack of function, catheter migration, fracture and hemorrhage. Recommendations for prevention and treatment of Hickman-catheter-related complications include the development of a select group committed to placement, daily maintenance and management of problems; prompt removal of catheters with *Candida* sp. fungemia and bacteremia due to *Bacillus* sp. or a bacteremia that persists for >48 h after initiation of appropriate antibiotics, tunnel infections or Hickman-catheter-associated thrombosis. The majority of bacteremias and exit site infections can be effectively treated with antibiotics and local care.

Key words: Hickman-catheter-related complications – Infectious complications – Noninfectious complications – Catheter-related bacteremias and fungemias

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Introduction

A major component of modern supportive medical care of the cancer patient is safe and reliable venous access for patients who need continuous-infusion chemotherapy, blood products, nutritional support and multiple courses of antimicrobial therapy [2]. Hickman catheters have prevailed at the University of Maryland Cancer Center (UMCC) as the major vascular access device used for patients with acute leukemia despite the introduction of additional methods. Patients with other types of hematological or solid tumors have also had Hickman catheters placed.

Studies have reported variations in management techniques and frequencies of Hickman catheter complications [8]. Our consistent philosophy has assumed that Hickman-catheter-related complications are preventable to a substantial extent. With the development of appropriate care and prevention techniques complications and malfunctions should decline [1]. We have, therefore, developed and participated actively in surgical placement, infectious disease care, Hickman catheter safety and patient education protocols in an attempt to standardize the insertion technique, management of catheter-related complications and daily maintenance procedures [4, 5, 12]. This involvement, coupled with prospective data collection, has provided a unique opportunity to examine the progression of Hickman-catheter-associated problems, to identify those factors that may minimize them, and to develop guidelines for the management and prevention of complications and malfunctions.

Hickman catheters have been the major venous access devices utilized at the University of Maryland Cancer Center from November 1978 to the present (Fig. 1). Data are reviewed through December 1987. Hickman catheters were inserted after consideration of the diagnosis of cancer, as adequate clinical rationale and the physical ability on the part of the patient, family member or guardian to maintain catheter patency and comply with care guidelines and infection prevention proto-

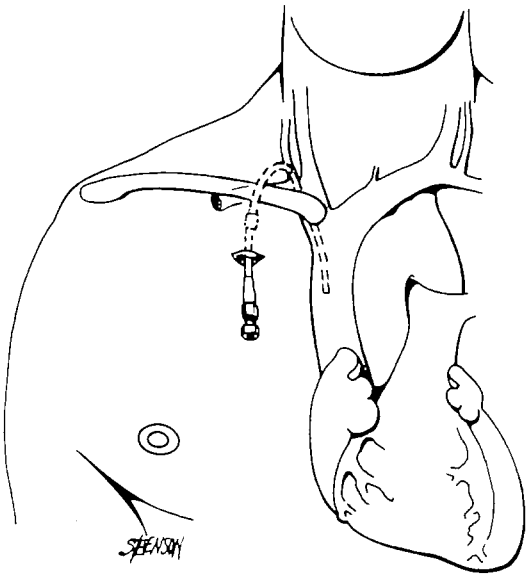

Fig. 1. Schematic diagram of Hickman catheter placement. The catheter is placed into the external jugular vein. From [11]

Table 1. University of Maryland Cancer Center: Hickman catheters 1978–1987

Total catheters	690
Patients	593
Diagnosis	
Acute leukemia	401
Initial induction	249
Remission	17
Relapse	135
Other cancer	289
Granulocyte count	
<100 PMN[a]/μl	156
100–1000 PMN/μl	113
Platelet count	
<50000/μl	230
50000–100000/μl	235
Catheter type	
Single lumen	312
Double lumen	378

[a] Polymorphonuclear neutrophils

cols. During periods of hospitalization, the oncology nursing service was responsible for Hickman catheter management but the patient or his/her family exclusively performed the daily outpatient care. Access into the Hickman catheters was unlimited and based on the clinical needs of the patient.

During the first 6 months of this study, a single surgeon inserted and removed all Hickman catheters. During the next 7 years, a second surgeon (W.P.R.) had the exclusive responsibility for insertion and removal of all Hickman catheters and was keenly involved in all catheter-related studies at the Cancer Center. This unique concern on the part of these two surgeons allowed for the uniform management of surgically related Hickman catheter issues during the first 7.5 years of this study. During the last 1.5 years of the study, Hickman catheters were placed and surgical complications were managed by a rotating group of general and vascular surgeons. A single oncologist (J.C.W.), who maintained consistent care guidelines, was primarily responsible for all decision-making relating to diagnosis and management of all Hickman-catheter-related complications. Throughout the entire study time, one nurse (K.A.N.) taught each and every patient or family member how to care for his or her Hickman catheter and was responsible for instructing nurses and physicians. The same nurse maintained a prospective record of each catheter, including patient demographics, Hickman catheter duration, granulocyte and platelet counts at time of placement, infectious and non-infectious catheter-related complications and other aspects related to the study such as chemotherapy and disease status. This nurse also provided the resource support for all Hickman-catheter-related questions and problems.

Catheter demographics

A total of 593 patients had 690 Hickman catheters placed at the University of Maryland Cancer Center between November 1978 and December 1987 (Table 1). The majority were placed in patients with acute leukemia (401 Hickman catheters). More than half were placed during initial induction therapy; 17 Hickman catheters were inserted during remission and 135 when the patient's leukemia was in relapse. Patients with other cancers received 289 Hickman catheters. The insertion of 156 Hickman catheters took place when the patient had a circulating granulocyte count below 100/μl. A total of 269 catheters were placed during neutropenia (below 1000/μl). A platelet count of 40000–50000/μl was required for Hickman catheter placement. However, despite pre-procedure platelet transfusions, 230 patients had platelet counts at the time of insertion below 50000/μl.

Of the 690 Hickman catheters, 312 had single lumens; the remaining 378 had double lumens. The initial two surgeons who were involved during the first 7.5 years of the study were responsible for placing the first 490 Hickman catheters while the rotating group of surgeons placed the remaining 200.

All Hickman catheters were inserted with the intention that they would remain in place as long as clinically needed. Consequently, Hickman catheters were not removed until there was a specific reason such as patient request, completion of therapy, complications requiring removal or patient death. Single-lumen Hickman catheters remained in place for a median of 127 days with a range of 1–1541 days; double-lumen catheters were in place for a median of 71 days with a range of 1–1715 days. The total number of Hickman catheter days for this 9-year study period was 134273. Single-lumen catheters accounted for 63528 days and double-lumen catheters the remaining 70745 days.

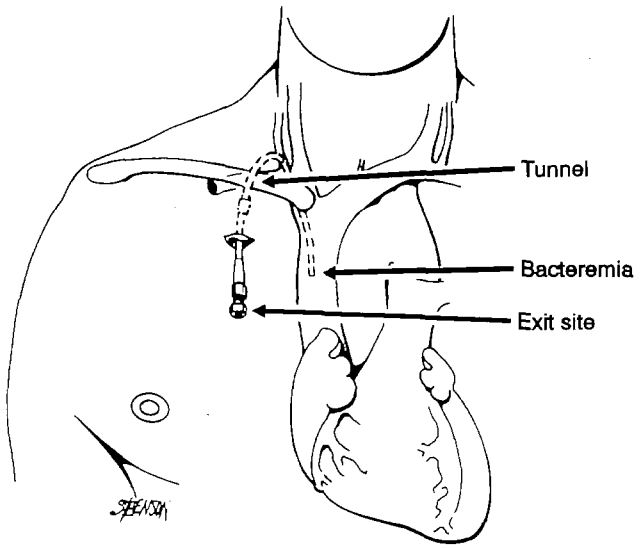

Fig. 2. Hickman catheter showing areas of exit-site infections and tunnel infections

Complications

Definitions

Complications were divided into infectious and non-infectious categories. Infectious complications included Hickman catheter exit-site infections, tunnel infections and catheter-associated bacteremias and fungemias (Fig. 2). Exit-site infections were defined as the development of erythema, tenderness, induration and/or purulence at the Hickman catheter exit site (a region extending from the subcutaneous Dacron cuff to the site of the catheter exit from the skin). Tunnel infections were defined as erythema, tenderness, induration and/or purulence along the subcutaneous tract from the Dacron cuff to the venotomy site. The area of involved tunnel varied from a few centimeters to the entire length of the catheter tract. Bacteremia among these patients was defined as clinical evidence of infection plus at least one positive blood culture. When the causative organism was a coagulase-negative staphylococcus, two positive blood cultures drawn from separate sites were required. All positive blood culture isolates were speciated but quantitative blood cultures were not done. A bacteremia was defined as being Hickman-catheter-related when a primary site could not be identified or signs and symptoms of a concomitant catheter exit-site or tunnel infection were present and the same organism was recovered from those sites of infection. All other bacteremias were defined as being unrelated to the Hickman catheter.

During the study period the most common non-Hickman-catheter-related sites of infection with accompanying bacteremia or fungemia included the lungs, pharynx, perirectal lesions and the skin.

Improvement with antibiotic therapy was defined as the resolution of bacteremia or fungemia and clinical signs and symptoms of infection. Hickman catheters were removed for infection if blood cultures were persistently positive or tunnel or exit-site infections continued despite appropriate antibiotic therapy.

Non-infectious complications

Non-infectious complications included thrombosis (diagnosed with a venogram of the involved extremity), loss of Hickman catheter function (i.e., the ability of the catheter to be aspirated and/or infused either temporarily or permanently), catheter migration from within the vessel, fracture of the catheter (usually the result of clamping with unprotected clamps) and accidental dislodgement of the catheter. Hemorrhage was defined as bleeding that necessitated a dressing change within the first 24 h of placement.

Infectious complications

Exit-site infections. There were 160 exit-site infections that occurred among the 690 Hickman catheters placed during this study (Table 2). These infections developed between days 1 and 1210 with a median time of onset 80 days after placement. Exit-site infections developed earlier with double-lumen catheters than with single-lumen catheters. The majority of exit-site infections usually occurred during periods of neutropenia with 100 of the 160 exit-site infections occurring while the patient was profoundly granulocytopenic (below 100/μl). The etiological organism was documented in only 59 exit-site infections. Gram-positive organisms were the most common pathogens, with *S. aureus* responsible for 35 infections. *P. aeruginosa* caused 8 exit-site infections, and 1 was due to *Candida* sp. Only 3 exit-site infections were due to *S. epidermidis.* Accompanying bacteremia occurred infrequently (13 occurrences), 6 of the 13 being due to *S. aureus.* Hickman catheter removal occurred in only 10 of 160 exit-site infections. Causative organisms for the infections that were difficult to treat included *P. aeruginosa, Candida tropicalis* (without fungemia) and *S. aureus.*

Table 2. University of Maryland Cancer Center: Hickman catheter exit-site infections 1978–1987

Total exit-site infections	160
Time to first infection (days)	80 (1–1210)
Single lumen	109
Double lumen	63
Granulocyte count	
< 100 PMN/μl	100
Infecting organisms	59
S. aureus	35 (6)*
S. epidermidis	3 (2)
P. aeruginosa	8 (2)
Candida sp.	1 (0)
Other	12 (3)
Treatment	
Antibiotics alone	150 (12)
Antibiotics plus removal	10 (1)

* Parentheses indicate bacteremia

Table 3. University of Maryland Cancer Center: Hickman catheter tunnel infections 1978–1987

Total tunnel infections	46
Time to first infection	70 (2–727)
Single lumen	98
Double lumen	30
Granulocyte count	
<100 PMN/μl	25
Infecting organisms	20
S. aureus	12 (8)[a]
S. epidermidis	2 (0)
P. aeruginosa	2 (0)
Other	4 (0)
Treatment	
Antibiotics alone	22
Antibiotics plus removal	24

[a] Parentheses indicate bacteremia

Table 4. University of Maryland Cancer Center: Hickman catheter bacteremias 1978–1987

Total bacteremias	397
Catheter-related	62
With exit-site infection	13
With tunnel infection	8
Non-catheter-related	335
Infecting organisms	
S. aureus	28 (2)[a]
S. epidermidis	62 (8)
P. aeruginosa	29 (18)
Bacillus sp.	8 (5)
Candida[b]	46 (21)
GNR[c] (*Enterobacteriaceae*)	111 (4)
Polymicrobial	25 (2)
Other	88 (3)

[a] Parentheses indicate removal
[b] 19 of 25 additional fungemias were persistent
[c] Gram-negative rods

Tunnel infections. Tunnel infections (Table 3) occurred in 46 of 690 catheters with a median time after catheter placement of 70 days, and a range from 2 to 727 days. Tunnel infections again were more common and occurred earlier with double-lumen than single-lumen Hickman catheters (a median of 30 days). The median number of days from placement to the occurrence of a tunnel infection was 30 days for double-lumen catheters and 98 days for single-lumen Hickman catheters. Of the 46 tunnel infections, 25 occurred during profound neutropenia. Pathogens were identified in 20 of the 46 infections, 12 of which were caused by *S. aureus*. Associated bacteremia occurred in 8 of the 20 total tunnel infections. The lack of clinical improvement with antibiotic therapy alone led to catheter removal in 24 of the 46 episodes of tunnel infection. Five additional patients with Hickman catheter tunnel infections were terminally ill at the time of diagnosis. Their catheters were not removed because of the palliative nature of their care. Excluding these latter 5 patients, only 17 of 41 tunnel infections could be managed without catheter removal. Unlike exit-site infections, the causative pathogen responsible for these tunnel infections appeared not to be a primary factor in the clearance of infection with antimicrobial therapy alone.

Bacteremias. There were 397 bacteremias and fungemias that occurred among patients who had Hickman catheters in place (Table 4); 62 were defined as catheter-related. Thirteen bacteremias were associated with exit-site infections and 8 with tunnel infections. The remaining 41 bacteremias were without an identifiable source and were defined as being catheter-related. The majority (335 of 397 bacteremias) were not catheter-related. *S. epidermidis* was the most frequently identified organism causing bacteremia, with 62 episodes. In only 8 instances of *S. epidermidis* bacteremia was catheter removal required for successful infection management. Catheters were removed in only 27 of 168 episodes of bacteremias with *S. aureus, P. aeruginosa* or enteric gram-negative bacilli. *Bacillus* sp. and *Candida* sp. followed a different pattern. *Bacillus* sp. bacteremia, while uncommon, was catheter-associated and 5 of 8 required catheter removal. Fungemia with *Candida* sp. was not uncommon, occurring among 46 catheter recipients, 21 of which had their catheters removed. Of the remaining 25 fungemias, 19 were persistent (lasting more than 3 days despite appropriate anti-fungal therapy).

We, like other institutions, have observed and reported an increase in *S. epidermidis* bacteremia during the past 10–15 years [13]. Whether or not these bacteresmias are related to the use of Hickman catheters or other vascular access devices remains unclear. At our institution, *S. epidermidis* bacteremia began to increase prior to the use of Hickman catheters and frequently originated from alimentary canal sites including the pharynx, esophagus and gut. However, studies have shown that *S. epidermidis* is capable of adhering to the inner lumen of siliconized rubber catheters. A study from the University of Maryland Cancer Center by Tenney et al. [10] reported the presence of gram-positive cocci imbedded in biofilm (Fig. 3) on the inner lumen of Hickman catheters after insertion. Prior to insertion, the catheters were shown to be free of any biofilm, but within 2–3 weeks after implantation, a continuous biofilm, identifiable by scanning electron microscopic evaluation had developed. The biofilm or glycocalyx is produced by slime-producing bacteria, most frequently *S. epidermidis. Candida* sp. and *Bacillus* sp. were two other organisms that were detected adhering to the inner lumen of the catheter, interposed within the glycocalyx with *S. epidermidis.* Despite the almost universal presence of adherent *S. epidermidis,* relatively few patients ultimately developed bacteremia or documented infection with this organism and thus the true clinical importance of these adherent bacteria remains unclear. In a subsequent study, utilizing molecular epidemiological techniques (i.e., plasmid profile and DNA restriction patterns), we showed that the bacteremic strains were much more likely to correlate with those organisms colonizing the alimentary tract than with either those adherent to the inner lumen of the Hickman catheter or those colonizing the skin [3]. This later work suggests that the alimentary tract and not the venous access device is the major site

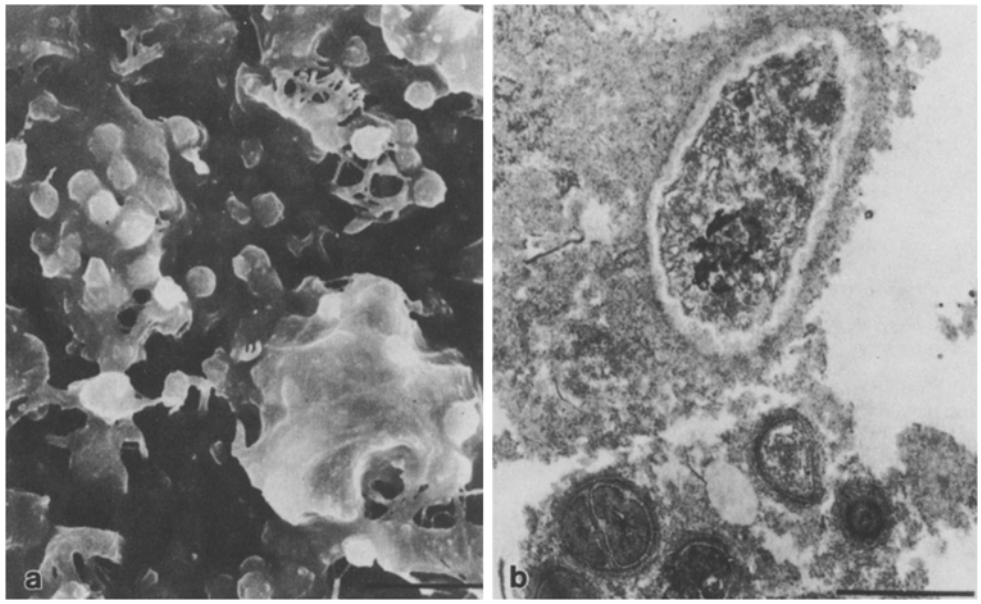

Fig. 3a, b. Scanning and transmission electron microscopic image of biofilm (bacteria and glycocalyx) on lumenal surface of segment of Hickman catheter. **a** Scanning electron micrograph showing gram-positive cocci in glycocalyx; **b** transmission electron micrograph showing cross-section of both gram-positive coccus and yeast. From Tenney et al. [10]

of origin of *S. epidermidis* bacteremia among neutropenic patients.

Non-infectious complications

There were 438 non-infectious complications occurring among these 690 catheters. Thrombosis occurred in 18 catheters requiring removal in 17. An intravenous venogram was the only reliable and reproducible method of diagnosis. There were 160 catheters that demonstrated at least a transient lack of function, usually in the ability to aspirate. Frequently this dysfunction was episodic or amenable to treatment with increased heparin flushes. Only 8 catheters required removal because of total blockage of flow. Catheter migration occurred in 13, although in 4 this displacement was minor. The remaining 9 Hickman catheter displacements were sufficient to warrant removal. Fracture of the catheter requiring repair occurred 124 times. Usually the catheter could be repaired with the application of silicone adhesive or replacement of the outer catheter hub. In 17 cases the catheter fracture could not be repaired and the catheter had to be removed.

Significant hemorrhage was infrequent despite the relative thrombocytopenia at the time of catheter placement. Except for 5 patients with concomitant disseminated intravascular coagulopathy in the early months of our experience, hemorrhage was never a major or life-threatening complication.

The complication rates of infectious and non-infectious complications for the University of Maryland Cancer Center's study were computed and compared to those in a review of 16 previously published reports by Press et al. [8] (Table 5). This review represented 292 more catheters than reported in our study but included only 63% of the total number of catheter days. The frequency of complications per 1000 days was somewhat higher at the University of Maryland Cancer Center with a rate of infectious complications of 1.9/1000 catheter days and a rate of 3.26 non-infectious complications/1000 catheter days. Of the 690 catheters placed at the University of Maryland Cancer Center, 321 had no complications for their entire duration of placement. It is important to note that our study included a large number of patients with acute leukemia (58%) who experienced repetitive episodes of chemotherapy-induced profound granulocytopenia and thrombocytopenia. Thus, the relatively low risk of complications in this patient group is remarkable.

Table 5. Complications of Hickman catheters: review of literature and UMCC experience 1978–1987

Institution	No. of catheters	Time in place (days)	Complications/1000 days	
			Infectious	Non-infectious[a]
Review[b]	982	84320	1.4	2.9
UMCC	690	134273	1.9	3.3

[a] Breakage, migration, accidental removal, hemorrhage, and thrombosis

[b] Compilation of 16 studies reviewed by Press et al. [8]

In an attempt to try to define associated potential risk factors further, we performed a multivariate analysis to assess the relative importance of certain factors for both infectious and non-infectious complications (Table 6). The double-lumen Hickman catheter and obesity (above 125% predicted weight) were shown to be significant risk factors for both infectious and non-infectious complications. This may be due at least in part to design features of the early double-lumen catheters. A groove was present between the lumens that interfered with closure of the exit site around the catheter. In addition, the cuff was relatively small and may have accounted for a higher incidence of catheter displacement. The new de-

Table 6. University of Maryland Cancer Center: risk factors for the development of Hickman catheter complications 1978–1987[a]

Conditions	Infectious		Non-infectious	
	RR[b]	*P*	RR[b]	*P*
Double-lumen	2.1	<0.01	3.6	<0.01
Single-surgeon	—	NS	0.77	<0.1
Obesity	1.7	0.02	2.0	<0.01
Granulocytopenia	1.6	0.02	—	NS

[a] Proportional-hazards regression model
[b] RR, Relative risk

sign of the double-lumen Hickman catheters resulted in a smooth contour, which eliminated problems with exit-site closure, and the larger cuff area seemed to minimize catheter migration. Non-infectious complications were fewer among those catheters inserted by the single surgeon, as compared to catheters inserted by the surgical group operating in rotation. Granulocytopenia at the time of the development of catheter-related infection was a significant risk factor for infection. It is worth noting that the utilization of prophylactic antibiotics had no impact on infectious complications in our study, nor in the study of Press et al. [8].

Recommendations

At the present time, the most important technique for improved Hickman catheter management is to have a select group of individuals who are committed to placement, daily maintenance care and management of catheter-related complications. This ensures continuity of patient care, education and the use of similar criteria for catheter removal in both infectious and non-infectious complications. Most infectious episodes can be handled without catheter removal. The majority of bacteremias are not catheter-related and can be effectively managed with antibiotic therapy alone. However, in all cases of *Candida* sp. fungemia and bacteremia due to *Bacillus* sp. or any bacteremia that persists for more than 48 h after initiation of appropriate antibiotics without an identifiable site, prompt catheter removal should be initiated. Tunnel infections appear to be much more difficult to manage without catheter removal and are associated with a higher frequency of bacteremia than exit-site infections. For this reason catheters should be promptly removed at the first evidence of tunnel infection. Exit-site infections are rarely associated with bacteremia and can usually be managed with antibiotics and local care without catheter removal. In general, 10–14 days of antibiotic therapy for exit-site infections is adequate.

Prompt Hickman catheter removal is recommended for the non-infectious complications of thrombosis. Short-term heparinization following catheter removal (10–14 days) is routinely used and recommended in all cases of documented thrombosis. Hickman catheters that become dislodged to the point that the tip is no longer in a large vessel also should be removed promptly. Other non-infectious Hickman catheter complications can be managed without removal. Now that mechanisms are available for Hickman catheter repair and lytic therapy, such as urokinase, the lack of function and catheter fracture should be rare etiologies for removal.

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