Management of Infection Associated with Total Hip Arthroplasty according to a Treatment Algorithm

S. G. Giulieri, P. Graber, P. E. Ochsner, W. Zimmerli

Abstract

Background: An algorithm for the management of hip arthroplasty-associated infections was validated in a cohort study.

Patients: 60 patients with 63 episodes of total hip arthroplasty-associated infections observed from 1985 to 2001 were included. The treatment algorithm was based on the time of manifestation, pathogenesis, and condition of implant and soft tissue. Three treatment options were proposed, namely debridement with retention, one-stage and two-stage replacement.

Results: The median patients' age was 72 years, the median follow-up 28 months; 29% were early, 41% delayed, and 30% late infections, 57% of the infections were exogenously and 43% hematogenously acquired. The overall success rate for the first treatment attempt was 83% (52/63). Patients treated according to the algorithm had a better outcome than the others (44/50 = 88% vs 8/13 = 62%, Relative risk (RR) 0.31, 95% confidence interval (CI): 0.11–0.86, $p < 0.03$); those treated with adequate antimicrobial therapy had a better success rate (87% vs. 50%, $p < 0.01$).

Conclusion: The proposed algorithm defines a rational surgical/antibiotic treatment strategy.

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Introduction

Infection associated with prosthetic joints is a dreaded complication of arthroplasty [1–5]. It occurs either by the exogenous route mainly perioperatively, or by the hematogenous route at any time after implantation [6, 7]. During *Staphyllococcus aureus* bacteremia, the risk of hematogenous seeding on hip prostheses has been shown to be 26% [7]. In our center, the infection rate during the 1st year after implantation was 0.4% in 1,570 consecutive patients receiving a primary hip replacement between 1984 and 2000 [8]. During the last few decades, the rate of exogenous infections has decreased due to the knowledge and modification of risk factors, the general use of antibiotic prophylaxis, and the improvement of aseptic techniques in the operating theater, e.g. by using laminar airflow technique [6]. However, the risk for hematogenous infection remains lifelong [7].

The goal of treatment of an infection associated with arthroplasty is the elimination of infection by conserving the functional integrity of the extremity. There are three different therapeutic procedures to reach this goal, namely debridement with retention of the device, one-stage exchange or two-stage exchange. Removal without reimplantation (Girdlestone hip) or lifelong suppressive antibiotic therapy do not conserve the functional integrity nor completely eliminate infection, and should therefore be avoided. In the only controlled study, the type of infection was well defined in terms of microorganism, stability of the implant, and time of infection [9]. Accordingly, the results of this study are only applicable to a minority of patients.

There is considerable debate regarding the optimal surgical treatment of infected arthroplasty, since no study compares the different surgical options. Such studies will probably never be performed, because of the low rate of infection and the great variability of clinical presentations and surgical approaches. Therefore, *Fisman* et al. [2] calculated the effectiveness of two different strategies for total hip arthroplasty-associated infections by using a Markov model to simulate the clinical course. According to their model, debridement and retention is a reasonable strategy to treat the elderly with staphylococcal or streptococcal infection, provided that their device is stable.

We have recently published an algorithm for the treatment of arthroplasty-associated infection, based on the interval after implantation (early, delayed, late), the type of

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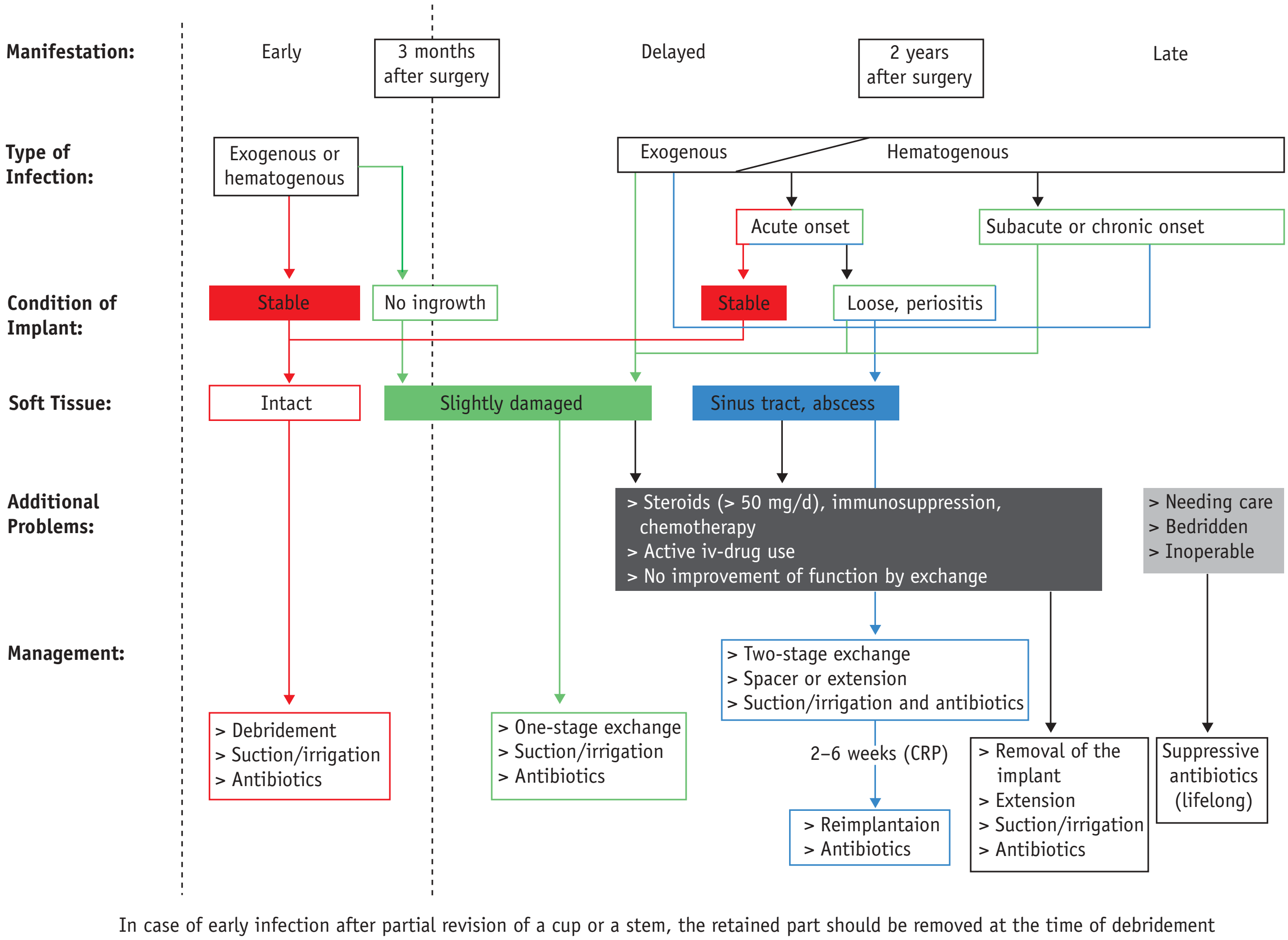

Figure 1. Algorithm for the surgical and antibiotic management of prosthetic hip-associated infection. Criteria for the decision are the postoperative lag, the type of infection, the condition of the implant and the soft tissue, as well as the comorbidity (from Zimmerli and Ochsner [10]).

infection (exogenous vs hematogenous), the condition of the implant, the soft tissue, and the patient's comorbidity (Figure 1) [10]. The aim of the present study was to retrospectively evaluate the clinical validity of this algorithm. For this purpose, we analyzed the data of 60 prospectively followed consecutive patients with 63 total hip arthroplasty (THA)-associated infections. Of these, 29 episodes occured in our cohort of 2049 consecutive patients [8], and 34 cases were referred.

Patients and Methods

Patients

From October 1984 to October 2001, 71 episodes of THA-associated infection were treated in 66 patients at the authors' institution. The Clinic of Orthopedic Surgery is a 48-bed unit acting as a primary care center for orthopedic surgery of the extremities, as well as a tertiary care center for patients who need revision arthroplasty. An Infectious Diseases Consultation Service has been available since 1994 by phone (Division of Infectious Diseases, University Hospitals Basel), and since 1999 by bedside consultation. All patients were prospectively followed at regular intervals. For the purpose of the study, the data were extracted from electronic files and from the charts [8]. One of the authors (SGG) evaluated all cases according to a protocol, in which demographic data, orthopedic case history, type of infection, signs and symptoms, laboratory parameters of inflammation (leukocyte differential counts, C-reactive protein, sedimentation rate) microbiology, histology, imaging procedures, surgical and antimicrobial therapy were documented.

Case Definition

A case was defined as THA-associated infection, if there was either a sinus tract communicating with the joint space (documented by arthrography or intraoperatively), or if at least two of the following criteria were met: (1) a positive bacterial culture of at least one intraoperative tissue specimen or the joint aspirate; (2) the presence of neutrophils in tissue specimens;

Table 1
Spectrum of infecting agents.

Agent	Episodes with implantation at our institution (n = 29)	Referred cases (n = 34)
Staphylococcus aureus	16 (55.3%)	11 (32.4%)
Coagulase-negative staphylococci	1 (3.4%)	10 (29.4%)
Streptococcus spp.	4 (13.8%)	3 (8.8%)
Enterococcus spp.	1 (3.4%)	1 (2.9%)
Gram-negative rods	1 (3.4%)	2 (5.9%)
Propionibacterium acnes	0	1 (2.9%)
Polymicrobial infection	4 (13.8%)	4 (11.8%)
Unknown microorganism	2 (6.9%)	2 (5.9%)

(3) clinical and laboratory signs of infection; (4) radiological signs of infection. We excluded cases with insufficient documentation, only postmortem diagnosis and infection after Girdlestone surgery, i.e. patients without implant at time of the planned study inclusion.

Analysis of Treatment

All cases were analyzed according to an algorithm which has been previously published, and which is presented in Figure 1. The first treatment attempt, performed in our center, was compared with the proposed algorithm, and cases were categorized into two groups, namely (1) treatment according to the algorithm, or more invasive therapy (e.g. two-stage instead of one-stage exchange), and (2) less invasive therapy (e.g. retention instead of exchange).

Antimicrobial treatment was reviewed for appropriateness by two investigators (W.Z., P.G.) and classified according to the following criteria: (1) adequate therapy: total duration of ≥ 3 months, duration of iv-therapy of ≥ 2 weeks, use of agent-appropriate drugs according to susceptibility testing and clinical studies, if available, use of antibiotics with efficacy against surface-adhering bacteria whenever possible [11–13], use of oral agents with good bioavailability; (2) partially adequate therapy: duration of at least 2 but less than 3 months, less than 2 weeks iv-therapy, (3) inadequate therapy: antimicrobial therapy not corresponding to the categories 1 and 2; (4) no antimicrobial therapy.

Outcome Definitions

Healing was defined as the lack of clinical signs and symptoms of infection, a C-reactive protein level < 10 mg/l or an erythrocyte sedimentation rate < 20 mm/h, and the absence of radiological signs of infection at the follow-up visit > 24 months after first revision. Probable healing was identically defined, but with a follow-up of < 24 months. New infection was a THA-associated infection with a new agent or new localization. Persistence or recurrence was defined as THA-associated infection with the same or unknown agent after the end of the antimicrobial therapy. Probable failure was a possible THA-associated infection after the end of therapy which did not fulfill the strict criteria for a THA-associated infection. Early death was a death < 14 days after hospitalization or first revision. Death due to sepsis was a death related to the THA-associated sepsis.

For outcome analysis, categories were grouped as follows: Success: healing, or healing from the original infection with later reinfection with a new microorganism. Failure: persistence or recurrence, probable failure, early death, death due to sepsis.

Statistics

Categorical data were evaluated with the χ^2-test or Fisher's exact test. Time to failure was estimated with the Kaplan-Meier method, and compared between groups by the log-rank test.

Results

Study Population

Out of 71 episodes in 66 patients, eight episodes were excluded for the following reasons: five had an infected Girdlestone hip at study entry, two episodes were only diagnosed at autopsy, and one episode was not sufficiently documented. 60 patients with 63 episodes were included.

The median age was 72 years; 33% of the patients were women. In 29 episodes, the initial THA was performed at our hospital, whereas 34 were referred from other institutions. Before infection, in 39 episodes (62%) the patients had no previous revision, in 18 episodes (29%) they had one, and in 6 episodes (10%) they had at least two previous revisions. The most common underlying condition was diabetes mellitus (14 cases, 22%), followed by cancer (four cases), iv-drug use (two cases), chronic renal failure with hemodialysis (one case), and rheumatoid arthritis (one case). One patient received 50 mg/d of prednisone.

Clinical Characteristics

18 episodes occurred in the early postoperative interval, i.e. within 3 months after surgery. All these infections were acquired by the exogenous route, since no other infectious focus with the same agent could be detected. Delayed infection, i.e. manifestation after three months until 2 years after surgery, was found in 26 episodes; 18 of them were exogenous, also labeled as low-grade infections. Finally, 19 episodes appeared more than two years after surgery, i.e. were late infections. In 12 episodes (19%), the presentation was acute, i.e. with a systemic inflammatory response syndrome. Symptoms at presentation included fever > 38 °C in 15 patients (25%), severe or major pain at rest in 49 (80%), local inflammation in 14 (22%), sinus tract or abscess in 32 (51%).

Microbiology

Table 1 summarizes the infectious agents of the 63 episodes. In 45 episodes (71%) intraoperative cultures (median six tissue specimens) yielded a causative agent, ten episodes were microbiologically documented with a culture of synovial fluid, and three with a deep sinus-tract culture.

Treatment

In 14 episodes (22%), the prosthetic joint was not removed. In 11 of them, revision surgery, i.e. synovectomy, control of stability of the implant, debridement and a 3-day course of irrigation/suction drainage was performed. In three episodes there was no revision or only minor surgery, due to the poor general condition of the patients.

One-stage exchange was the initial intervention in 16 (26%) episodes, while two-stage exchange was chosen in 31 (49%) episodes. Debridement and irrigation/suction drainage was performed in each case with exchange arthroplasty. The median duration of time from device removal to reimplantation was 24.5 days (range 12–165 days). Finally, two episodes were treated with a definite removal of the implant, i.e. with a Girdlestone hip. After initial surgery for infection, wound revision was performed 11 times. Table 2 summarizes the characteristics of the antimicrobial therapy. Adequate or partially adequate antimicrobial therapy was administered in 55 episodes (87%).

Table 2
Characteristics of the antimicrobial therapy.

	No. of episodes (%)	Median days of treatment (range)
Adequate	40 (64%)	
Partially adequate	15 (23%)	
Inadequate	7 (11%)	
No treatment	1 (2%)[a]	
Duration of antibiotic treatment		101 (0–360)
≥ 90 days	47 (75%)	
Duration of iv treatment		29 (0–126)
≥ 14 days	50 (79%)	
Type and duration of oral treatment[b]		
Ciprofloxacin alone	10	75 (21–124)
Ciprofloxacin + rifampin	24	78.5 (12–360)
Betalactam	8	35 (2–180)
Other	9	78 (15–182)

[a]Death at day 2 after surgery; [b]Eleven episodes were not orally treated and one patient was not treated at all (early death)

Outcome

The median duration of follow-up after the first revision was 28 months (range, 0–156 months). One patient died 2 days after surgery. The overall success rate was 83% (52 of 63 episodes). 50 episodes (79%) could be followed for > 24 months. Among these patients, a definite cure was documented in 42 cases, resulting in a success rate of 84% (42 of 50 episodes) in all patients who completed a follow-up of at least 24 months. Four patients had reinfection at another site or with another microorganism after healing of the original infection. Seven patients died without any signs of infection before they had their 2-year follow-up visit. Among the 11 episodes in patients with treatment failures, eight had persistent or recurrent infections with the same or an unknown agent, two died (one of sepsis and the other of postoperative complications), and one had a possible failure. Table 3 summarizes the success rate according to the type of infection, to the different surgical techniques, and to the adherence to the algorithm. The outcome was not statistically different in patients with different types of infection (early, delayed, late), as well as with different routes of inoculation (exogenous, hematogenous). Regarding the type of surgery, the success rate in patients with retention without debridement was significantly lower than in those with one- or two-stage replacement. Retention with debridement had a success rate of 64% overall, and of 71% if the indication was chosen according to the algorithm (Figure 1).

Patients surgically treated according to the algorithm or more invasively had a better outcome than patients with less invasive intervention. Cure rates were 88% and 62%, respectively ($p < 0.03$), with a relative risk for treatment failure of 0.31 (95% CI 0.11–0.86). Figure 2 shows the Kaplan-Meier plot of failure-free survival.

Table 3
Outcome according to characteristics of infection, type of surgical treatment and adherence to algorithm.

	Success rate
Infection type	
Early	14/18 (78%)
Delayed	23/26 (88%)
Late	15/19 (79%)
Pathogenesis	
Hematogenous	21/27 (78%)
Exogenous	31/36 (86%)
Type of surgical treatment	
Retention with debridement	7/11 (64%)
Retention without debridement	1/3[a]
One-stage replacement	15/16 (94%)
Two-stage replacement	28/31 (90%)
Girdlestone operation	1/2
Adherence to algorithm	
According to or more invasive	44/50 (88%)[b]
Less invasive	8/13 (62%)

[a] $p < 0.05$ vs one-stage and vs two-stage exchange; [b] $p < 0.03$ vs less invasive treatment

The success rate was significantly higher in patients with at least partially adequate antimicrobial therapy (48/55, 87%) than in those with inadequate or without antibiotic therapy (4/8, $p = 0.01$). Patients treated according to the algorithm and with at least partially adequate antimicrobial therapy had the highest success rate (42/45, 93%).

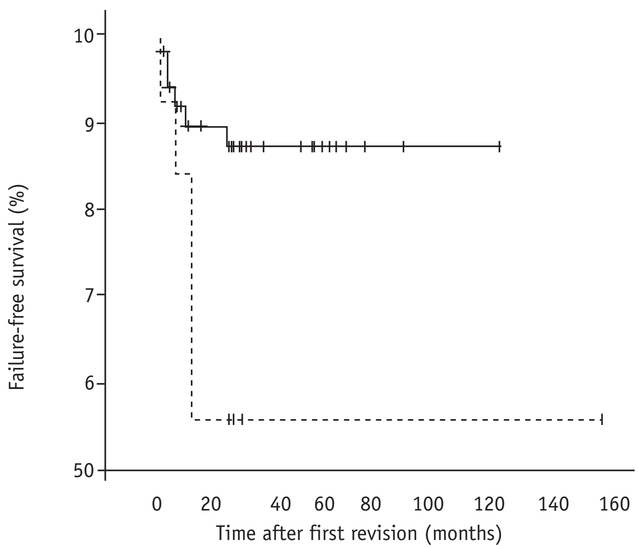

Figure 2. Kaplan-Meier estimates of the cumulative risk of failure according to the surgical treatment group. Solid line represents the group of patients treated according to the algorithm or more invasively (n = 50). Dotted line represents the group of patients treated less invasively than proposed in the algorithm (n = 13). The risk of failure was lower in the patients treated according to the algorithm or more invasively than in patients with less invasive treatment ($p = 0.023$, log-rank test).

From 1994 an Infectious Disease Service by phone was instituted, which was replaced with an in-house consultation service in 1999. There was a trend toward a better outcome among infections treated during the last 8 years of the study period (1994–2001: success rate 42/48, 88%) compared to the success rate during the first 9 years (1985–93: 10/15, 67%, $p = 0.06$).

Discussion

Infections associated with THA have variable presentations, thus not allowing all of them to be treated identically according to one single protocol [1, 2, 10]. This variability includes pathogenesis (exogenous vs hematogenous), duration of infection, stability of the implant, soft-tissue condition, type of microorganism and its susceptibility pattern. It is still unclear whether two-stage replacement is better than one-stage exchange, or debridement with retention, since these different options have not been tested in a randomized fashion in a homogenous patient group. The choice of the surgical approach depends on personal experience, the concept of the surgeon, as well as on results of published case series. We evaluated a recently published treatment algorithm, in which we defined the patients qualifying for the different surgical options [10, 14, 15]. This algorithm has been developed to retrospectively analyze the patient cohort. Thus, we asked the question whether the criteria for the different surgical procedures were supported by clinical experience. The strengths of this study are the prospective data collection in an electronic database, and the management by a specialized team in a single institution [8, 9 ,11–16]. The weakness is the lack of randomization to a surgical procedure, which would allow an unbiased evaluation of different surgical options. However, such a design is not feasible.

The spectrum of infecting agents was similar to the very large case series of the Mayo Clinic involving 578 patients with prosthetic joint infection [4]. In our series, staphylococci were found at a similar frequency as in *Steckelberg's* series [4] (60% vs 53%). However, in our study, *S. aureus* infection was more frequent (43% vs 23%), and coagulase-negative staphylococci were less frequent (17% vs 30%). Streptococci (11% vs 9%) and gram-negative bacilli (5% vs 6%) were equally frequent. Thus, the infecting agents in our study population were representative.

The main result of our study is the observation that each type of infection could be treated with similar success, provided that the optimal treatment option was chosen. Adherence to the proposed algorithm resulted in a significantly better outcome than non-adherence (88% vs. 62% success rate, $p < 0.03$). Since debridement with retention, one-stage exchange or two-stage exchange did not have a significantly different outcome, if the appropriate procedure was chosen, there is no need to favor two-stage exchange in each THA-associated infection, despite the fact that the latter procedure seems to be more safe from a theoretical point of view. Retention without debridement had a lower success rate than the other procedures, and therefore does not represent a reasonable treatment option.

As shown in the Kaplan-Meier curve of failure-free survival, relapses are most frequent during the 1st year, but can occur up to about 2 years. Therefore, a 2-year follow-up is important. In our study, 79% of the episodes were followed > 24 months. The success rate was similar in patients with > 24 months of follow-up, and in the whole study population.

In the literature, there are case series for each surgical procedure. Debridement with retention is the most critical procedure, if the patients are not carefully chosen. Unfortunately, in most centers, this technique is not chosen according to positive preselected criteria, but mainly used in patients refusing the exchange of the infected implant. Thus, success rates as low as 14% have been reported [17]. The conclusion in the study of *Crockarell* et al. [17] was that retention should not be attempted in patients who have a chronic THA-associated infection, since this approach universally fails. Based on these negative results, as well as on better results in selected patient populations (68–100% success rate) [9, 18, 19], debridement with retention should be strictly reserved for patients with a short history of infection, with a stable implant, with an infecting agent susceptible to an antimicrobial agent acting on surface-adhering microorganisms [11–13, 15], and with good compliance to long-term (3 months) therapy.

The published success rates in patients with one-stage replacement of an infected hip prosthesis are between 76% and 100% [20–27]. In order to obtain a fair result, the one-stage exchange should be reserved for patients with reasonable soft-tissue conditions and with a microorganism susceptible to an antimicrobial agent with good bioavailability.

The success rate of the two-stage exchange is between 73% and 97% [28–31]. This procedure should be used in patients not qualifying for the less invasive options. In our study, we generally used a spacer between the two surgical procedures. During the last few years, the interval between prosthesis removal and reimplantation was kept short, i.e. 2–4 weeks. However, in patients with difficult-to-treat microorganisms, such as enterococci or any type of multidrug-resistant bacteria, we prefer a 6-week interval without implantation of a spacer, between the two procedures. These patients were kept on limb extension until reimplantation. If patients with two-stage exchange had a 6-week course of antibiotics prior to joint reimplantation, and if the intraoperative cultures show no growth after an adequate drug-free interval, we stop the antimicrobial therapy, provided that the histology of intraoperative biopsies does not show any signs of acute inflammation, i.e. granulocytic infiltrates. Otherwise, the treatment should be continued for a total of 3 months.

In most published studies, the type of antimicrobial therapy is not reported in detail. In our study, we defined it as adequate, partially adequate or inadequate according to the above-mentioned criteria. In 87% of the patients, the treatment was at least partially adequate, with regard to the choice of antimicrobial agents and duration of iv and oral therapy. These patients had a significantly better outcome than the others (87% vs 50% success, $p = 0.01$). The best outcome (93% success) was observed in the 45 patients who were treated according to the algorithm and with at least partially adequate antimicrobial therapy.

In conclusion, this cohort study validates the predefined criteria for the choice of the appropriate surgical procedure and antimicrobial therapy for THA-associated infection. Thus, the previously published treatment algorithm offers a guideline for rational therapy [10].

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