■ HIP

Prevention of periprosthetic joint infection

NEW GUIDELINES

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The World Health Organization (WHO) and the Centre for Disease Control and Prevention (CDC) recently published guidelines for the prevention of surgical site infection. The WHO guidelines, if implemented worldwide, could have an immense impact on our practices and those of the CDC have implications for healthcare policy in the United States.

Our aim was to review the strategies for prevention of periprosthetic joint infection in light of these and other recent guidelines.

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Periprosthetic joint infection (PJI) is currently the leading cause of failure for primary and revision total knee (TKA) and total hip arthroplasty (THA).[1,2] As the number of arthroplasties which are performed each year increases, so does the number of patients with PJI, with some predicting an annual rate of between 38000 and 270 000 PJIs in the United States by the year 2030.[3,4]

The management of PJI requires specific resources and carries a heavy financial and psychological burden.[3] Despite extensive research the most effective strategies for prevention of PJI remain unknown. An International Consensus Meeting (ICM) was held in 2013 to identify the best practices for prevention of PJI.[5] Several organisations have subsequently proposed evidence-based guidelines for the prevention of surgical site infections (SSI).

The World Health Organization (WHO) and the Centre for Disease Control and Prevention (CDC) have recently revised their evidence-based guidelines for the prevention of SSI. The WHO guidelines[6] are the first international evidence-based guidelines for the prevention of SSI and cover 23 topics. The CDC guidelines[7] address 13 fields, as an extension of their previous guidelines which were published in 1999, including a section dedicated to the prevention of PJI. Both guidelines answer key questions based on the best available evidence. Other notable and comprehensive guidelines are the expert document, sponsored by the Society for Healthcare Epidemiology of America (SHEA)[8] and the National Institute for Health and Care Excellence (NICE) guidelines in the United Kingdom.[9]

The goal of this review is to discuss the prevention of PJI with reference to these recently released guidelines.

Pre-operative measures

These can be found in Table I.

Nasal decolonisation. Approximately 30% of SSIs are attributed to *Staphylococcus aureus* (*S. aureus*). The rate of nasal colonisation by *S. aureus* is about 25% and there has been an increase in the rate of methicillin resistant *S. aureus* (MRSA) in recent years.[10] The observation that *S. aureus* colonisation correlates with increased risk for SSI[11,12] has led to implementation of pre-operative screening and decolonisation protocols for *S. aureus*. While universal screening is a subject of much debate,[13,14] the use of intranasal mupirocin for decolonisation has been considered acceptable as a means of decreasing the rate of SSIs. A recent study of 9690 patients screened pre-operatively for *S. aureus* showed a rate of reduction of SSIs of nearly 70% from 1.11% to 0.34%.[15] The logistics regarding screening and decolonisation, as well as the presence of conflicting reports, has prevented the authorities from making a definitive recommendation regarding this issue. The future for *S. aureus* decolonisation may be improved by the use of effective iodine or chlorhexidine based agents, that avoid the potential for the emergence of antibiotic resistance, and can be used as a single application.[16]

Guidelines: While both the WHO and the CDC provide no recommendations regarding the pre-operative screening for *S. aureus*, the WHO recommend using mupirocin 2% for treating known nasal carriers (strong recommendation).[6]

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Table I. Pre-operative recommendations for the prevention of surgical site infection, according to various guidelines

	ICM[5]	WHO[6]	CDC[7]	SHEA[8]	NICE[9]
Nasal screening and decolonisation	Against universal screening. Mupirocin choice of therapy in known carriers (strong).	Mupirocin 2%, with or without antimicrobial body wash; choice of therapy in known carriers (moderate).	Not covered.	Screen and decolonise before high risk procedures (moderate).	Against routine decolonisation.
Pre-operative skin preparation	Use CHG (or antiseptic soap when unavailable) starting at least the night before surgery (strong).	Shower or bathe (moderate). Unresolved: the efficacy of antimicrobial soap or impregnated cloth.	Shower or bathe with plain or antimicrobial soap or an antiseptic agent at least the night before surgery (IB). Unresolved: best timing, type of wash or antimicrobial impregnated cloth.	Unresolved whether CHG is effective.	Bathe or shower using soap either the day before or the day of surgery, with no evidence showing the efficacy of pre-operative washing. Unresolved whether CHG is effective.
Immunosuppressive therapy	Immunosuppressive therapy should be stopped (strong).	Do not stop immunosuppressive therapy routinely (very low).	Unresolved: the effect of specific treatments, duration, dose or peri-operative management.	Avoid immunosuppressive medications in the peri-operative period, if possible (low).	Not covered.
Glycemic control (including peri-operative recommendations)	Glucose level < 200 mg/dl and HbA1C < 7% (strong).	Use protocols for glycemic control in both diabetic and non-diabetic patients (low). No conclusion regarding glucose target levels.	Maintain glucose level < 200 mg/dL (IA) in both diabetic and non-diabetic patients. Unresolved: efficacy of tighter glycemic control, the best timing, duration or method to reduce SSI, or HbA1C target.	Lower haemoglobin A1c ≤ 7% before surgery (high). Immediate post-operative ≤ 180 mg/dL. Against tighter control (≤ 110 mg/dL) (moderate).	Against routine insulin for non-diabetic patients post-operatively.

ICM, International Consensus Meeting (strength of consensus); WHO, World Health Organization (quality of evidence); CDC, Center for Disease Control and Prevention (strength of recommendation); NICE, The National Institute for Health and Care Excellence; SHEA, Society for Healthcare Epidemiology of America (quality of evidence); CHG, chlorhexidine; IA/IB, strong recommendations; II, weak recommendations; SSI, surgical site infection

They do not recommend for or against the use of a chlorhexidene body wash for the purpose of decolonisation.

Pre-operative skin cleansing. This is intended to decrease the bacterial load. Many authors have shown that whole body skin cleansing pre-operatively reduces the incidence of subsequent SSI.[17] The optimal time to start cleansing and the most appropriate agent to be used remains unknown. Cleansing can be performed using an antibacterial or an antiseptic soap, wash cloth, or antibacterial liquid. Chlorhexidene is probably the best agent for cleaning as it has activity against many pathogens including MRSA.[18] Another unresolved issue is the region of the body that needs to be cleaned. It is logical to assume that cleaning the whole body, as recommended by the CDC,[7] leads to a more effective reduction of the bacterial load.

Guidelines: Based on the available evidence, the ICM, WHO and CDC all recommend that skin cleansing pre-operatively should be undertaken. Most agree on the effectiveness of pre-operative cleansing, at least the night before surgery, and that the whole body should be cleaned.[5-7]

Intra-articular injections. Intra-articular injections of corticosteroids are used widely as part of the non-operative treatment of osteoarthritis. One of the adverse outcomes of such treatment is the potential for contamination of the joint by bacteria and subsequent infection. A time dependent analysis of the Humana data set between 2007 and 2014, involving patients who received an injection to the knee before TKA, showed a higher rate of infection among 29 603 who had an injection pre-operatively compared with 54 081 who did not (4.4% *versus* 3.6%, odds ratio (OR) 1.23).[19] The authors did not perform a multivariate analysis, limiting the relevance of the findings. Studies on injections to the hip before THA have also shown an increased risk of post-operative infection,[20] but a recent systematic review failed to reach a conclusion.[21]

Guidelines: The issue regarding the risk of contamination during an intra-articular injection and the potential for subsequent PJI remains unresolved. The CDC guidelines[7] visited the issue but made no conclusive recommendations.

Immunosuppressive therapy. Patients with rheumatoid arthritis or other inflammatory diseases, who are on disease modifying agents (DMARDs), have been suggested to have an increased risk of PJI following total joint arthroplasty (TJA).[22] The increased rate of PJI poses unresolved challenges regarding the peri-operative management of DMARDs, with no clear recommendations.[23] A recent analysis of the risk factors for SSI among 227 patients with rheumatoid arthritis who underwent 332 elective orthopaedic operations showed no significant correlation to treatment with DMARDs.[24]

Guidelines: While the ICM recommended that the DMARDs be stopped prior to elective arthroplasty, based on the half-life of the drugs,[5] the WHO recommended that they should not routinely be discontinued (weak recommendation).[6] The decision should be made for each patient individually. This issue remains unresolved in the CDC guidelines.[7]

Table II. Antimicrobial recommendations for the prevention of surgical site infection, according to different guidelines

	ICM[5]	WHO[6]	CDC[7]	SHEA[8]	NICE[9]
Pre-operative					
Timing	Within 1 hr (2 hrs for Vancomycin/Clindamycin) (strong).	Within 2 hrs, while considering its half-life (moderate).	Based on its pharmacokinetics, it reaches bactericidal levels when incision is made (IB).	Within 1 hr (2 hrs for Vancomycin/Fluoroquinolones) (high). Closer to incision more effective. No conclusion on the relation to tourniquet.	Single dose at start of anesthesia, considering its pharmacokinetics. Before inflation of tourniquet.
Weight adjustment	Should be weight adjusted (strong).	Not covered.	No conclusion.	Adjust to patient weight (high). 80 kg ≤ 2 g of cefazolin 120 kg ≤ 3 g.	Not covered.
Intra-operative					
Re-dosing	After two half-lives of the prophylactic antibiotics and in cases of large blood volume loss (> 2000 cc) and fluid resuscitation (> 2000 cc) (strong).	Not covered.	No conclusion.	If the duration of the procedure exceeds two half-lives of the drug or there is excessive blood (high).	After two half-lives of prophylactic antibiotics.
Post-operative					
Timing	No longer than 24 hrs post-operatively (strong).	Against antibiotics after surgical wound is closed (moderate).	Against antibiotics after surgical wound is closed (IA).	No longer than 24 hrs post-operatively (high).	Not covered.
Drain	Do not continue antibiotics (strong).	Do not continue antibiotics (low).	Do not continue antibiotics (IA).	Do not continue antibiotics (high).	Not covered.

ICM, International Consensus Meeting (strength of consensus); WHO, World Health Organization (quality of evidence); CDC, Center for Disease Control and Prevention (strength of recommendation); NICE, The National Institute for Health and Care Excellence; SHEA, Society for Healthcare Epidemiology of America (quality of evidence); IA/IB, strong recommendations; II, weak recommendations

Peri-operative measures

Glycemic control. Between 8% and 22% of patients who undergo TJA have diabetes,[25] and about one third have undiagnosed hyperglycemia.[26] Diabetes, especially when uncontrolled, is a significant risk factor for SSI.[27] Even non-diabetic patients who develop hyperglycaemia post-operatively have a significantly increased risk of SSI,[28] with SHEA recommending that post-operative glucose levels be maintained < 180 mg/dL. The identification of patients with diabetes or hyperglycemia and the implementation of strict peri-operative glycaemic control minimises the risk of infection following various surgical procedures.[29]

Guidelines: Both the WHO and the CDC[5,7] note the importance of strict glycaemic control at the time of surgery, regardless of the diagnosis of diabetes. The CDC recommends that the fasting level of glucose in the blood of patients undergoing surgery be < 200 mg/dL (strong recommendation).[7]

Peri-operative antibiotic prophylaxis. This is shown in Table II.

The importance of prophylactic antibiotics in the prevention of SSI has been well established.[30] First-generation cephalosporins cover most bacteria responsible for orthopaedic infections.[31] In patients with a high risk for MRSA colonisation, such as those institutionalised in nursing homes or dialysis units, additional vancomycin or teicoplanin may be used.[32] According to a recent report from Europe,[33] teicoplanin was the most common agent used in high risk patients; 84% of practices reported using it alone or in combination with gentamicin. The ideal time to start antibiotics remains controversial.[34,35] Most agree that prophylaxis should end within the hour before surgery, requiring some agents such as vancomycin, with a longer infusion time, to be started a few hours earlier. The ICM recommended that the dose of peri-operative antibiotics should be based on weight and that prolonged treatment should be considered in procedures with a long operating time and those with excessive blood loss.[36,37] Although several guidelines have addressed the benefit of prophylactic antibiotics, a recent study from three Australian centres[38] reported almost 40% non-compliance with guidelines. This rate was especially high in regard to the adjustment of the dose by weight and prolonged treatment. Non-compliance was associated with a higher risk of SSI.[38] Finally, there is evidence that continuing antibiotic treatment beyond 24 hours is not essential and could lead to increased bacterial resistance.[39,40]

Guidelines: these are similar regarding recommendations for, and the timing of, prophylactic antibiotics based on individual pharmacokinetics. The WHO and the CDC do not address types of pre-operative antibiotics, prolonged treatment or the indications for prophylactic treatment. They recommend that the antibiotic should not be continued beyond wound closure (strong recommendation) even in the presence of a surgical drain.[5,7]

Intra-operative measures

These are shown in Table III.[41]

Laminar air flow. While these systems have been shown to reduce bacterial load and decrease the rate of SSI,[42] other studies failed to show that a decrease is SSI is cost effective,[43] making their use questionable.

Table III. Intra-operative recommendations for the prevention of surgical site infection (SSI), according to various guidelines[41]

	ICM[5]	WHO[6]	CDC[7]	SHEA[8]	NICE[9]
Laminar air flow	Not necessary (strong).	Against (low to very low).	Not covered.	Follow the American Institute of Architects recommendations (low).[41]	Not covered.
Body exhaust suit	Cannot recommend .	Not covered.	Unresolved.	Not covered.	Not covered.
Operating room traffic	Minimum (strong).	Not covered.	Not covered.	Minimum (low).	Minimum.
Intra-operative skin preparation	Acknowledge the importance of alcohol (strong). Unresolved: optimal solution.	Alcohol-based CHG agent (low to moderate).	Alcohol based antiseptic agent (IA).	Dual agent containing alcohol (unless contraindicated) (high).	Unresolved: optimal solution.
Hair removal	Use clippers if necessary, as close to surgery as possible (strong).	Against hair removal. Use clippers if necessary (moderate).	Not covered.	Against hair removal (moderate). If necessary, use clippers outside the operating room.	Against hair removal. If necessary, use clippers with a single-use head on the day of surgery.
Sealant and drapes	Unresolved.	Against (very low).	Not necessary (II).	Against (high).	Against routine use of non-impregnated incise drapes.
Oxygenation	Not covered.	Recognise the significance in endotracheal intubation. 80% fraction for 2 to 6 hrs post-operatively (moderate).	Recognise the significance in endotracheal intubation and recommend administrating increased FiO_2 intra-operatively and in the immediate post-operative period (IA). Unresolved: other types of anesthesia, duration, target level or delivery method.	Supplemental oxygen during and immediately post-operatively with mechanical ventilation (high).	Maintain saturation rate ≥ 95%. Do not recommend routine supplemental.
Normothermia	Recognise the significance of patient normothermia (strong).	Suggest the use of warming devices in the operating room (moderate).	Recognise the significance (IA). Unresolved: method, timing, and lower limit.	Maintain normothermia during the peri-operative period when anesthesia duration ≥ 1 hr (high).	Recognise the significance and add specific guidelines.
Antibiotic impregnated bone cement	Agree on its effectiveness. Recommend when high-risk PJI (strong).	Not covered.	Unresolved is the effect on biofilm.	Not covered.	Not covered.
Wound irrigation	Agree on irrigation (strong). Unresolved is the optimal solution.	Consider aqueous iodophor solutions. Against antibiotic irrigation (low).	Use aqueous iodophor solutions for deep or subcutaneous tissue irrigation (II). Unresolved: antimicrobial irrigation.	Perform antiseptic wound lavage (moderate).	Against irrigation.
Coated sutures	Unresolved on whether specific sutures or staples prevent infection.	Suggest Triclosan-coated sutures (moderate).	Against the use of antimicrobial coated sutures (II).	Against routine use of antimicrobial coated sutures (moderate).	Unresolved on whether this may reduce the SSI risk. The type of surgery may influence.
Wound dressing	Occlusive dressings with alginated hydrofiber (weak).	Against the use of any kind of advanced dressing (low).	Unresolved.	Not covered.	Unresolved. Suggest silver nylon might be better than gauze.
Topical antimicrobial agents	Not covered.	Not covered.	Against. PRP is not necessary for SSI prevention (II).	Against (moderate).	Against.
Allogeneic blood transfusion	Increases the risk for PJI (strong).	Not covered.	Against withholding transfusion of necessary blood products (IB). Unresolved is whether blood transfusion is an independent risk factor and if there is an association with volume or specific products.	Increases the risk of SSI by decreasing macrophage function. Reduces blood loss and the need for blood transfusion (moderate).	Not covered.

ICM, International Consensus Meeting (strength of consensus); WHO, World Health Organization (quality of evidence); CDC, Center for Disease Control and Prevention (strength of recommendation); NICE, The National Institute for Health and Care Excellence; SHEA, Society for Healthcare Epidemiology of America (quality of evidence); PJI, periprosthetic joint infection; IA/IB, strong recommendations; II, weak recommendations; PRP, platelet-rich plasma

Orthopaedic space suits. Earlier studies showed that the use of body exhaust suits based on the Charnley system reduce the risk of PJI.[44] The principle behind this system is to extract the air from the clean operating room through the suits to the outside based on negative pressure. Modern space suits and helmets, however, do not follow the same principles. Consecutive studies from the New Zealand registry suggest that modern systems do not decrease the incidence of PJI and might even increase the risk of infection.[43,45]

Operating theatre traffic. The rationale behind limiting personnel and movement in the operating theatre is to reduce the shedding of pathogens from the skin of personnel and contamination of the air as a result of air entering from outside.[46]

Guidelines: All agree that operating theatre traffic should be kept to a minimum. The WHO, based on low quality evidence, recommend that laminar air flow should not be used (weak recommendation).[6] The CDC does not comment on the issue of the optimal environment in the operating theatre.[7]

Surgical site preparation. Various agents can be used to prepare the site of surgery.[47] Although there are studies which report the superiority of one agent over another, many are of poor methodology with comparative arms which were not equal.[48] The presence of alcohol in the preparation agent is clearly important.[49] Dual-preparation of the skin should be considered, as contamination can occur during draping. A recent randomised double-blinded study involving 577 patients reported significantly less SSI when skin was prepared twice before and after draping, rather than once, with an alcohol based Povidone-iodine-I as an antiseptic agent (1.8% *versus* 6.5%, p = 0.02).[50]

Guidelines: There is agreement that alcohol must be involved in the preparation of the surgical site (strong recommendation).[5-7]

Skin sealant and drapes. Plastic drapes have been used at the site of the incision intra-operatively with the understanding that this practice leads to a reduction of SSI. Newer drapes are impregnated with bacteriostatic agents such as iodine or chlorhexidine and are believed to reduce bacterial proliferation during surgery as well as isolate the skin edges from potential contamination.[51] The use of drapes without antiseptic agents has been shown to increase the risk of SSI.[52,53] NICE recommend the use of iodine impregnated drapes,[9] and recent studies support their use.[51,54] Nevertheless, the issue regarding the use of draping the area of the incision in general and the need for draping with bactericidal or bacteriostatic agents remains unresolved. A recent prospective, randomised study on 96 patients undergoing joint preservation surgery noted that the rate of skin contamination was significantly higher in patients without a drape in place compared with those with a drape (12.5% *versus* 27%, OR 2.48).[55]

Guidelines: The WHO and CDC do not feel that draping the area of the incision is necessary, based on low quality evidence (weak recommendation).[6,7] There are, however, current studies[5,51,53] which show that draping the area may reduce SSI.

Normothermia and oxygenation. Ensuring normal body temperature and oxygenation by maintaining normal blood flow to the site of surgery may reduce the risk of SSI.[56,57] Normothermia during surgery also provides an optimal milieu for the immune system.[58] The means of achieving these goals include the use of pre- and intra-operative warming devices and the administration of pre-warmed intravenous fluids.[59] The best way to ensure normothermia remains unknown. Concerns regarding the use of air warming and the potential for contamination have been raised by a few authors although this has not been proven.[60] Supplying increased fraction oxygen (FiO_2) increases the partial pressure of oxygen and may theoretically decrease the risk of SSI.[61]

Guidelines: These guidelines agree on the importance of maintaining the normothermia of the patient during surgery and the administration of supplementary oxygen (strong recommendation).[5-7]

Antibiotic impregnated bone cement. Previous data from the Norwegian registry,[62] and subsequent meta-analyses[63] suggested that the use of antibiotic impregnated polymethylmethacrylate (Abx-PMMA) resulted in a lower incidence of infection and all time failure following THA.[62,63] New data from the Australian registry[64] regarding patients who have undergone THA or TKA with Abx-PMMA are not as convincing, with no difference in the incidence of infection being recorded.[64] In the absence of convincing data, the ICM recommended that Abx-PMMA be used only for high risk patients undergoing TJA.[5]

Guidelines: Most guidelines do not specifically address this issue. The CDC did not reach any recommendations regarding the use of Abx-PMMA during elective arthroplasty.[7]

Wound irrigation. Theoretically, wound lavage removes dead tissue and bacteria. There is general consensus regarding the use of intra-operative irrigation, although the efficacy and type of irrigation of deep and superficial tissues is inconclusive. Povidone-iodine appears to be efficient and safe,[65] with no improved bacterial removal from the addition of antibiotics.[66]

Guidelines: The WHO and CDC recommend that the incision be washed with aqueous iodophor solutions (weak recommendation).[6,7]

Wound dressing. The wound is a possible point of entry for bacteria resident on the skin or in the environment.[67] Different types of advanced dressing have been suggested to decrease this risk by isolating the incision or by the administration of local antimicrobial agents.[68,69] Given the increased cost of these dressings and the potential development of bacterial resistance and side effects, their routine use is not advised.

Guidelines: This issue is mostly unresolved, with broad differences between guidelines based on low evidence studies. The WHO recommends not using any type of advanced dressing (weak recommendation).[6]

Post-operative measures

Blood transfusion. A recent meta-analysis reported a prevalence of SSI of 2.88% in patients who undergo TJA and received an allogenic blood transfusion compared with 1.74% among those who did not.[70] This supports earlier studies that showed a two-fold greater risk for PJI in patients who have a transfusion.[71,72] Pre-operative screening of haemoglobin levels and the use of erythropoietin aim to maximise the levels of haemoglobin. Intra-operative methods such as thorough haemostasis, the use of a tourniquet and of topical or intravenous tranexamic acid, and reducing the operating time, all aim to reduce blood loss and the need for transfusion.[23] Other methods such as the use of platelet-rich plasma have not been shown to be effective.[73] In recent years there has been a move to initiate transfusion for symptomatic patients and avoid using the level of haemoglobin as a trigger.[71]

Guidelines: Although visited, the most effective measures for conserving blood and the potential for the adverse

effects of blood transfusion on the incidence of SSI remain unresolved in the CDC guidelines.[7]

Wound complications. Haematoma formation and the prolonged drainage of the wound are considered to be risk factors for the development of a PJI, in that they provide fertile ground and a pathway for bacteria to grow and invade the joint.[74] Thus, good haemostasis, and water-tight wound closure are believed to be important in reducing haematoma formation and wound drainage.[75] The use of potent anticoagulation has also been shown to be associated with problems relating to the wound and subsequent PJI.[76,77] In order to minimise the risk of infection, the appropriate management of these complications is extremely critical. There are a number of strategies that include the application of compressive dressing, vacuum-assisted devices, the evacuation of a haematoma, and even a one-stage exchange arthroplasty.[78] The ICM stated that the management of patients with wound related complications is not an emergency and all effort should be made to optimise the patient pre-operatively.[79] This includes the correction of anaemia, the control of hyperglycaemia and reversal of anticoagulation agents. Potent anticoagulation may affect wound healing, further raising the importance of considering milder, but effective agents, such as aspirin for thromboembolic prophylaxis.[80,81]

Guidelines: The CDC guidelines address the use of anticoagulation and the risk of SSI without reaching any conclusions.[7]

Discussion

The new guidelines provide important updates and new recommendations for the prevention of SSI by addressing certain issues. However, due to the lack of evidence in many areas, they fail to be comprehensive. Questions regarding common practices, such as nasal screening, remain unanswered. These guidelines do, however, raise awareness about evidence-based medicine and may minimise the widely inappropriate use of antibiotics that contributes to the emergence of antimicrobial resistance.[82] The guidelines also call for the design of controlled studies that will yield data regarding many common practices for which evidence is scarce.

Take home message:

- The WHO and the CDC recently published evidence-based guidelines for the prevention of SSI.
- The new guidelines provide important updates and new recommendations for the prevention of SSI but due to the lack of evidence in numerous areas, the guidelines fail to be comprehensive.
- These guidelines will hopefully help in setting a standard of care based on best evidence available and call for the design of controlled studies that will yield data regarding many common practices for which evidence is lacking.

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