

BMJ Open Controlling methicillin-resistant *Staphylococcus aureus* (MRSA) in a hospital and the role of hydrogen peroxide decontamination: an interrupted time series analysis

Brett G Mitchell,^{1,2} Wilhelmine Digney,³ Phil Locket,³ Stephanie J Dancer⁴

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¹Faculty of Nursing and Health, Avondale College of Higher Education, New South Wales, Australia

²School of Nursing, Midwifery and Paramedicine, Australian Catholic University, Dickson, Australian Capital Territory, Australia

³Launceston General Hospital, Launceston, Tasmania, Australia

⁴Department of Microbiology, Hairmyres Hospital, UK

Correspondence to

Dr Brett G Mitchell;
brett.mitchell@avondale.edu.au

ABSTRACT

Objectives: The impact of surface disinfection versus detergent cleaning on healthcare associated infection rates remains unresolved. We aimed to evaluate the efficacy of hydrogen peroxide (HP) decontamination against methicillin-resistant *Staphylococcus aureus* (MRSA).

Design: Single centred retrospective before and after study design.

Setting: Launceston General Hospital, Tasmania, Australia.

Participants: Patients with MRSA infection or colonisation.

Interventions: Rooms occupied by patients with MRSA infection or colonisation were cleaned following discharge with either detergent or HP.

Main outcome measures: MRSA room contamination following cleaning; new MRSA acquisition in patients.

Results: Over 3600 discharge cleans were completed, with more than 32 600 environmental swabs processed. MRSA was isolated from 24.7% rooms following detergent cleaning and from 18.8% of rooms after HP ($p < 0.001$). The incidence of MRSA acquisition reduced from 9.0 to 5.3 per 10 000 patient days in detergent and disinfectant arms, respectively ($p < 0.001$).

Conclusions: Use of HP disinfection led to a decrease in residual MRSA contamination in patient rooms compared with detergent. It may also have encouraged the reduction in patient MRSA acquisition despite several confounders including staff feedback on terminal cleaning, additional MRSA screening and quicker laboratory methods. Infection control is best served by concurrent interventions targeting both the patient and healthcare environment.

INTRODUCTION

There is no single remedy for controlling hospital-acquired infections (HAIs), although current evidence supports a multifaceted approach.^{1–3} Understanding the transmission modes of infectious agents and applying basic

Strengths and limitations of this study

- The large number of environmental swabs taken over a long period is a key strength of this study.
- The ability to measure methicillin-resistant *Staphylococcus aureus* (MRSA) contamination and acquisition in a consistent manner over a long period of time is also a strength.
- We were able to examine several potential confounders, not always possible when analysing infection control interventions.
- Limitations include the two different processes for application of HP disinfectant in the study, since a vapourised disinfectant cannot be delivered in shared patient areas.
- Additional MRSA screening of inpatients was initiated during the study and this could also have had an effect on the overall outcome.

infection prevention and control principles are critical for reducing HAIs.⁴ One fundamental requirement for preventing transmission in healthcare environments is environmental cleanliness, since the environment serves as a reservoir for potential pathogens. Several studies have shown that if a patient is admitted to a room previously occupied by a patient colonised or infected with a particular organism, presumed environmental persistence increases the acquisition risk for that patient with the same organism.⁵ Colonisation pressure is also thought to play a role in the transmission of hospital organisms.^{6–9} Additional studies have shown that enhanced cleaning significantly decreases environmental contamination of a range of HAI pathogens.^{10–14} These studies, alongside those evaluating colonisation pressure, demonstrate the potential importance of the environment in infection transmission and prevention.¹⁵

Divergent opinions prevail as to whether surface disinfection is required for routine cleaning as opposed to detergent cleaning.¹⁶ This translates into considerable variations in practice, which complicates the overall assessment of hospital cleaning methods. Controversy over best practice and materials as well as the role of cleaning itself as an important control intervention has received recent comment.^{17–20} Thus, the impact of surface disinfection versus detergent cleaning on HAI rates remains scientifically unresolved, despite a growing body of literature.^{19 21} This paper describes a study that evaluated the efficacy of hydrogen peroxide (HP) decontamination alongside patient monitoring and screening against methicillin-resistant *Staphylococcus aureus* (MRSA) HAI rates in an Australian hospital via a two-armed initiative. MRSA was chosen as the target pathogen because screening programmes for this organism are already well established, and environmental persistence makes it vulnerable to the cleaning process. MRSA is a reliable indicator of overall hygiene practices in hospitals.^{14 22}

METHODS

Study design

A retrospective before and after study design was used, to assess the efficacy of HP decontamination versus use of a detergent alone for terminal cleaning, with a focus on MRSA patient acquisition and environmental load.

Setting

The study was conducted at Launceston General Hospital, a 300-bed public hospital providing acute care facilities for residents of Launceston and the northern region of Tasmania, Australia. Every year the hospital treats over 24 000 inpatients and 225 000 outpatients. The hospital provides a range of treatments and services including emergency care, intensive care, acute and elective surgery and renal services. The study was conducted between 1 January 2006 and 31 December 2012.

Interventions

Rooms accommodating MRSA patients were cleaned following discharge. Between 1 January 2006 and 30 October 2009, the rooms were cleaned twice with a pH neutral detergent (mixed in warm water) and referred to as the 'detergent arm' in this paper. From 1 November 2009, an initial clean using detergent was performed, followed by the application of HP, herein referred to as the 'disinfectant arm'. In single rooms, HP (6%) vapour decontamination was conducted using the dry hydrogen vapour room decontamination system (Nocospray, EquipMed, North Ryde, New South Wales, Australia) according to the manufacturer's instructions. In shared rooms, HP was applied to surfaces using a cloth, as per the manufacturer's instructions. The product used was Oxivir TB 0.5% (Diversey, Smithfield, New South Wales, Australia). Both Nocospray and Oxivir TB are registered with the Australian Therapeutic Goods

Administration as a hospital grade disinfectant. The cleaning staff responsible for cleaning MRSA patient rooms were provided with appropriate documented training. Cleaning staff were in-house hospital employees and not contractual staff.

Outcomes

The main outcomes for this study were identification of MRSA from surfaces in the patient room following the discharge clean, and the incidence of hospital-acquired (HA) MRSA bacteraemia and HA MRSA acquisition throughout the hospital for the period under study.

Identification of MRSA from patient rooms

Following a discharge clean, nine environmental swabs were taken from each of the following sites: ceiling vent, sink, console, bed, patient/visitor chair, patient table, bedside locker, mattress and the pillow (following pillowcase removal). The console is fixed to the wall behind the patient's bed and includes the oxygen supply and patient call bell system. Swabs were taken by rolling a swab, premoistened with sterile saline (0.9%), over the designated surfaces and subsequently inoculated onto MRSA agar plates (further details below). The same environmental swabbing procedure was used throughout the study period, and those persons responsible for undertaking the environmental swabs remained constant throughout the study.

Identification of patients with MRSA

An established patient screening programme identified MRSA, whether colonised and/or infected. Persons admitted to the hospital during the study period were screened on admission for MRSA if they were nursing home residents; interhospital transfers; or shared a room with a person with known MRSA. Samples were collected using a premoistened swab (with sterile saline) from the nose, throat and perineum. From January 2010, all inpatients who remained in hospital also received weekly MRSA screens. During 2010 and 2011, compliance with admission and weekly MRSA screening was monitored by reviewing all persons with MRSA admitted to the hospital against laboratory testing undertaken, with the hospital achieving 80% compliance or higher. Infection control staff were notified of positive MRSA results by the laboratory on a daily basis. The results and patients were reviewed by infection control staff. Patients with a laboratory result indicating MRSA (screen or other specimen), with no history of MRSA and negative admission screen were deemed to have acquired MRSA. MRSA-positive patients were nursed with contact precautions and either isolated in a single room or placed in a room with other patients known to have MRSA. Patients were not actively decolonised with nasal creams and/or antiseptic body washes.

An episode of HA MRSA bacteraemia was defined as an MRSA-positive blood culture, taken 48 h or longer after admission. Only the first isolate per patient was

counted, unless at least 14 days passed without additional positive culture. Monthly numbers of HA MRSA were collected in addition to the number of patient bed days. The monthly incidence of HA MRSA per 10 000 patient care days was calculated. Monthly counts of patients who acquired MRSA (colonisation and/or infection) during the study period were determined. The monthly incidence of MRSA acquisition per 10 000 patient care days was subsequently calculated.

Microbiology laboratory methods

The microbiology laboratory performing relevant testing during the study is an accredited laboratory (National Association of Testing Authorities). In March 2009, the laboratory changed from a mannitol salt and oxacillin agar plate (PP2131 Oxoid Adelaide, South Australia, Australia) to Brilliance chromogenic agar (Oxoid, Adelaide, South Australia, Australia). Brilliance MRSA Agar was directly inoculated from screening swabs. Plates were allowed to warm to room temperature before inoculation—for 20 h (minimum) at 37°C. Each plate was divided into quarters to enable multiple swabs to be cultured. This pragmatic approach was implemented in the interests of cost, given the large number of swabs taken in this study. The issue of potential cross-contamination from multiple inoculations is in part reduced by the primary data analysis undertaken, since we explored whether any MRSA was present, rather than being site specific. Additionally, one plate was used per patient or room, so there would be no cross contamination. Environmental and patient swabs were not inoculated onto the same plates. The appearance of denim blue colonies suggested that MRSA and confirmatory tests were performed, including antimicrobial susceptibilities.

Bias

We identified several potential confounders in evaluating the effect of disinfectants on MRSA acquisition and room contamination. Room contamination may be affected by the competency of staff performing the clean, as well as the efficacy of vapourised HP at penetrating different surfaces. To overcome these, the staff involved in the use of HP were limited, received competency-based training and were supervised by the researchers. An external quality control process was also undertaken by the manufacturer. Rooms cleaned with vapourised HP were validated by using test strips specific to that product. The test strips were used intermittently throughout the study to identify any issues with application.

Acquisition of MRSA may be affected by hand hygiene compliance and also by antimicrobial consumption. Hand-hygiene compliance was monitored shortly after the introduction of the HP intervention and then continued throughout, in accordance with a national approach to hand-hygiene monitoring.²³ Antimicrobial consumption was recorded in order to identify changes in antibiotic usage associated with MRSA, consistent with national and international approaches.²⁴

Data analysis

Data analysis was performed in SPSS V.20.0.²⁵ The comparison between the presence or absence of MRSA in a room for the two arms was undertaken using univariate analysis. Fisher's exact test (2 tail) was used to compare the presence of MRSA in rooms following discharge between the two arms. Time series analysis was subsequently applied to the data (also in SPSS V.20.0) with a lag variable to allow for autocorrelation between monthly measurements. The key variable of interest is the change in cleaning approach. This analysis was repeated for the overall proportion, and the proportions, for each surface.

The comparison of MRSA bacteraemia and MRSA acquisition between the two periods was performed using Fisher's exact test to determine any difference in the total incidence between these two arms. To explore this further, time series analysis was performed to examine the monthly incidence of MRSA bacteraemia and acquisition individually.

RESULTS

Environmental contamination

Three thousand six hundred and twenty-nine discharge cleans were undertaken: 1917 in the detergent arm and 1712 in the disinfectant arm. There were 32 661 environmental swabs processed during the entire study period. **Table 1** summarises MRSA detection from each environmental site during the study period, for both the detergent and disinfectant arms.

In rooms that were cleaned with a detergent, MRSA was recovered from at least one site for 473 of 1917 (24.7%) rooms cleaned. This is a higher recovery rate compared with 322 of 1712 (18.8%) rooms cleaned with HP ($p < 0.001$). **Figure 1** illustrates the monthly proportion of rooms that had MRSA identified from at least one site during the study period. Of the 1712 rooms cleaned with HP, 349 were manually cleaned with 0.5% HP and 1363 with 6% vaporised HP using an automated system.

Results for the overall proportion of rooms identified with MRSA following a discharge clean were analysed using time series (regression). Assessment of the residuals of these models indicated no further serial correlation or deviations from the assumptions of normality and homogeneity. A significant positive autocorrelation was found, suggesting that the level of MRSA in the previous month was indicative of the following month. There was a small reduction in the overall proportion of MRSA with the HP intervention, with a drop of 0.035 or 3.5% (95% CI 0.4% to -7.5%). This result was borderline non-significant ($p = 0.08$).

MRSA acquisition

The incidence of MRSA bacteraemia reduced from 0.16/10 000 patient care days (95% CI 0.04 to 0.35) in the detergent arm to 0.11/10 000 patient care days

Table 1 Univariate analysis comparing MRSA environmental contamination following cleaning with detergent and disinfectant over a 6-year period in one 300 bed hospital

Object	Detergent			Disinfectant (HP)			p Value
	No MRSA	MRSA	Per cent MRSA	No MRSA	MRSA	Per cent MRSA	
Vent	1803	114	6.3	1622	90	5.5	0.39
Sink	1815	102	5.6	1640	72	4.4	0.12
Console	1799	118	6.6	1602	110	6.9	0.78
Bed	1703	214	12.6	1572	140	8.9	<0.01
Chair	1755	162	9.2	1565	147	9.4	0.90
Table	1761	156	8.9	1597	115	7.2	0.11
Locker	1786	131	7.3	1605	107	6.7	0.50
Mattress	1762	155	8.8	1604	108	6.7	0.04
Pillow	1824	93	5.1	1643	69	4.2	0.26

HP, hydrogen peroxide; MRSA, methicillin-resistant *Staphylococcus aureus*.

(95% CI 0.02 to 0.30) in the HP arm. This reduction was not significant ($p=0.58$). There was also a reduction in the incidence of MRSA colonisation and infection during the two arms, from 334 cases (9.0/10 000 patient days) to 186 cases (5.3/10 000 patient days). This reduction was statistically significant ($p<0.001$) and was confirmed using time series analysis of the monthly incidence of MRSA acquisition ($p<0.001$) (figure 2).

DISCUSSION

There are two main findings from this study. First, the introduction of more stringent terminal cleaning using HP led to a decrease in residual MRSA contamination in patient rooms, compared with detergent alone (table 1; figure 1). Second, following the introduction of HP, there has been a reduction in the rate of new MRSA patient acquisitions throughout the hospital. Both of these findings will be discussed in detail.

The decrease in the number of rooms found to have MRSA following a terminal clean with HP is

unsurprising given the antibacterial properties of this agent. However, there are additional analyses to consider. Univariate analysis compared the total proportion of rooms found to have MRSA in each arm, demonstrating a significant reduction in MRSA. This method does not account for changes over time, particularly if there are confounders. Time series analysis is required to address this point. The proportion of rooms found to have MRSA each month were analysed over time and the two arms compared. This showed a reduction in MRSA contamination after terminal cleaning ($p=0.08$). It is also worth noting that while there appears to be a reduction after the intervention, there exists unexplained variability before the intervention, which contributes to general uncertainty over the observed change during the study period (figure 1).

Systematic screening showed that the bed was the only item in the patient's room where a significant reduction in residual MRSA was found. Given that the majority of rooms were cleaned with vapourised HP, a potential

Figure 1 Presence of methicillin-resistant *Staphylococcus aureus* following terminal cleaning, 2006–2012.

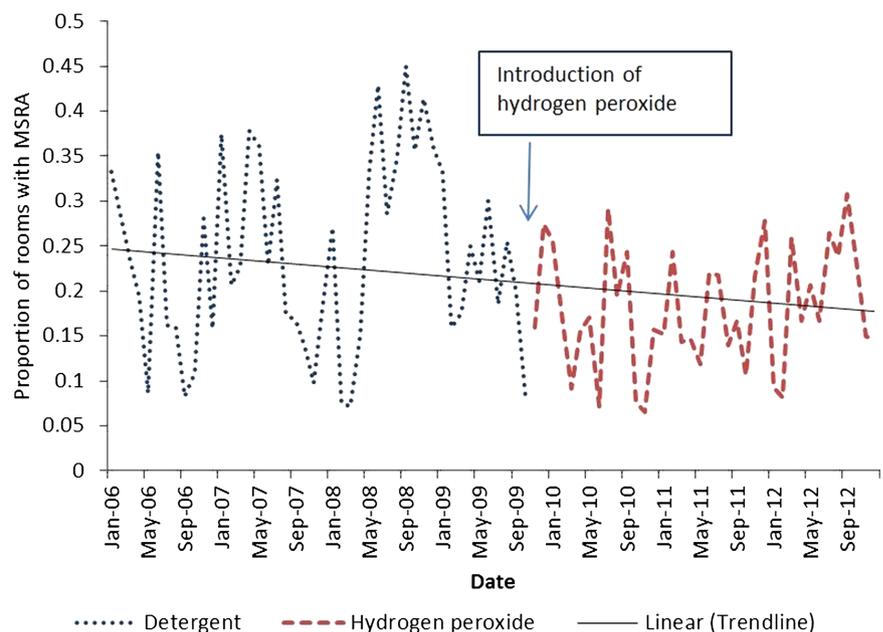
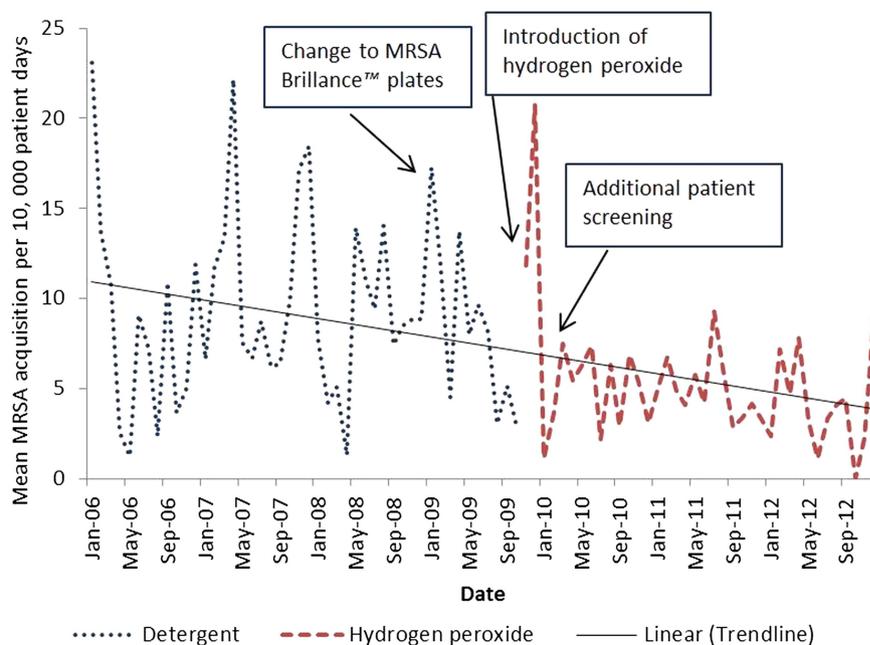


Figure 2 New methicillin-resistant *Staphylococcus aureus* acquisitions, 2006–2012.



explanation for this could be the positioning of the unit in the room. There was little or no reduction in MRSA contamination for the majority of screened items, so we cannot be completely confident that HP was directly associated with widespread reduction in MRSA contamination. It is also important to note that the intervention did not just involve the introduction of HP, but also represented monitoring and feedback to the cleaning and clinical staff. Environmental data were regularly issued to staff and to the hospital executive. This process also occurred during the detergent arm of the study. The introduction of HP was led by the infection control team, with a staff member in this team dedicated to overseeing its use. In addition, the number of people responsible for discharge cleaning was reduced in the disinfectant arm, making feedback more feasible. It is possible that discussion of the methods and importance of cleaning plus feedback all played an important part in the improvements seen.²⁶

This study also found a reduction in the amount of new MRSA acquisitions in the hospital. As with all interventions of this nature, the impact of additional changes other than cleaning over the study period cannot be excluded. Potential confounders include enhanced screening activity, change in laboratory methods and antimicrobial consumption. At about the same time as the introduction of HP decontamination, there was an increase in admission and ongoing screening effort. All inpatients who remained in hospital received weekly MRSA screens in addition to more active admission screening. It is possible that (1) more persons with MRSA acquisition were identified following the introduction of weekly screens, and (2) additional admission and ongoing screening, resulting in more patients, afforded contact precautions. This should have reduced the potential for cross transmission, but there was no

intervention other than contact precautions for newly identified patients with MRSA.

Different laboratory methods for MRSA detection were not thought to have had a significant impact on isolation rates from either patients or the environment; both agar types encourage growth of MRSA under standard laboratory conditions. However, use of chromogenic agar reduces the time required to isolate MRSA from specimens, which would speed up control interventions for positive patients during this study. This may have had an impact on transmission risk if patients were identified earlier than they would have been with the original method.

Regarding antimicrobial consumption, data on fluoroquinolone and cephalosporin usage were as obtained from the hospital's pharmacy department from 1 January 2009 to 30 December 2011 for each month. These were converted into the internationally recognised drug usage rate daily defined doses (DDD)/1000 bed-days.²⁴ While most antibiotics encourage MRSA shedding and spread between patients, exposure to these particular antibiotic classes are more likely to be associated with increasing MRSA acquisition rates.^{27–29} Between 1 January 2009 and 30 October 2009, mean DDDs of fluoroquinolone and cephalosporin agents were 98.9 (95% CI 96.3 to 101.6) and 50.9 (95% CI 49.0 to 52.8) per 1000 bed-days, respectively. From 1 November 2009 until 31 December 2010, mean DDDs of fluoroquinolone and cephalosporins were 67.6 (95% CI 66.6 to 68.8) and 56.3 (95% CI 55.1 to 57.6) per 1000 bed-days, respectively.³⁰ There was therefore a significant reduction in fluoroquinolone usage ($p < 0.001$) alongside a significant increase in cephalosporin use ($p < 0.001$), both of which may have affected the MRSA acquisition rate during the study.

A further consideration is the impact of any changes in hand hygiene compliance. Early in the study period

(2009), a national hand hygiene initiative was introduced in the hospital including monitoring of hand hygiene compliance from early 2010, consistent with the 'Five moments' model.²³ There was no statistical increase in hand hygiene compliance when comparing data from April 2010 to data at the end of 2012. Specifically, hand hygiene compliance was 66.9% (95% CI 64.9% to 68.6%) in early 2010, compared with 70.4% (95% CI 68.3 to 72.5%) at the end of 2012.^{31 32} Further, a critical element of the national hand hygiene programme, the introduction of alcohol-based hand rub in patient care areas, had already been in place since 2006.

STRENGTHS AND LIMITATIONS

The large number of environmental swabs, collected over a long period of time in a systematic manner, is a key strength of this paper. We are unaware of any other study that has examined such a large number of environmental swabs when evaluating the use of a disinfectant and detergent. A second strength of this study was the ability to measure MRSA acquisition in a consistent and robust manner, via admission and weekly patient screening. Additionally, this study had the ability to examine data on potential confounders, not always possible when analysing infection control interventions.

A limitation of this study is the use of two different processes in the delivery of HP-vapour and application by cloth. The reason for using these two processes was due to the inability to release vapourised HP in shared patient areas. In defence of this, we raise two points. First, the aim of the study was to compare the use of a detergent and disinfectant on MRSA contamination and subsequent acquisition, not a comparison of different applications of a disinfectant. This would be the logical next step in future studies, exploring the most appropriate methods for disinfectant use. Second, as MRSA acquisition was examined at a hospital level, it would not be possible to determine the relative effects of the two methods used to apply HP.

Sufficient data were unavailable to evaluate the cost-effectiveness of implementing HP in this study. The introduction of HP in any hospital may have some additional costs, potentially offset by increases in hospital efficiency. Future studies evaluating the introduction of a new cleaning intervention should consider whether the intervention is cost-effective.

CONCLUSION

In conclusion, we assessed the efficacy of terminal HP decontamination versus detergent alone by monitoring the postclean environmental load alongside MRSA patient acquisition. Introduction of disinfectant cleaning led to a decrease in residual MRSA contamination in patient rooms, compared with detergent. There was also a reduction in the rate of new MRSA acquisitions throughout the hospital. After considering potential confounders, we propose that the reduction in the

MRSA acquisition rate was the result of several initiatives, including disinfectant cleaning, focus on terminal cleaning (including staff feedback), additional MRSA screening, quicker laboratory methods and isolation. The relative contribution of all of these is unknown. Infection control is best served by concurrent interventions targeting both the patient and healthcare environment.

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Competing interests None.

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Data sharing statement All the data used in this study are available from Avondale College for Higher Education, Faculty of Nursing and Health subject to ethical approval. Please contact BM (brett.mitchell@avondale.edu.au) if interested in accessing the data.

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