


# Aspergillus in COVID-19 intensive care unit; what is lurking above your head?

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Sue Dailly<sup>1</sup>, Erin Boatswain<sup>2</sup>, Julie Brooks<sup>1</sup>, Glen Campbell<sup>3</sup>, Katy Dallow<sup>4</sup>, Ahilanandan Dushianthan<sup>2,5,6</sup>, Sarah Glover<sup>4</sup>, Melanie Griffiths<sup>2</sup>, Sanjay Gupta<sup>2</sup>, James Austin<sup>4</sup>, Robert Chambers<sup>2</sup>, Sarah Jeremiah<sup>1</sup>, Charlotte Morris<sup>2</sup>, Nitin Mahobia<sup>1,4</sup>, Martyn Poxon<sup>3</sup>, Alison Rickman<sup>4</sup>, Helen Jaques<sup>4</sup>, Tatshing Yam<sup>4</sup> and Kordo Saeed<sup>4,5,6</sup> 

## Abstract

**Introduction:** Through routine respiratory samples surveillance among COVID-19 patients in the intensive care, three patients with aspergillus were identified in a newly opened general intensive care unit during the second wave of the pandemic.

**Methodology:** As no previous cases of aspergillus had occurred since the unit had opened. An urgent multidisciplinary outbreak meeting was held. The possible sources of aspergillus infection were explored. The multidisciplinary approach enabled stakeholders from different skills to discuss possible sources and management strategies. Environmental precipitants like air handling units were considered and the overall clinical practice was reviewed. Settle plates were placed around the unit to identify the source. Reports of recent water leaks were also investigated.

**Results:** Growth of aspergillus on a settle plate was identified the potential source above a nurse's station. This was the site of a historic water leak from the ceiling above, that resolved promptly and was not investigated further. Subsequent investigation above the ceiling tiles found pooling of water and mould due to a slow water leak from a pipe.

**Conclusion:** Water leaks in patient areas should be promptly notified to infection prevention. Detailed investigation to ascertain the actual cause of the leak and ensure any remedial work could be carried out swiftly. Outbreak meetings that include diverse people with various expertises (clinical and non-clinical) can enable prompt identification and resolution of contaminated areas to minimise risk to patients and staff. During challenging pandemic periods hospitals must not lose focus on other clusters and outbreaks occurring simultaneously.

## Keywords

Aspergillus, COVID-19, SARS-CoV-2, outbreaks, intensive care

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<sup>1</sup>Infection Prevention and Control, University Hospital Southampton NHS Foundation Trust, Southampton, UK.

<sup>2</sup>Intensive Care, University Hospital Southampton NHS Foundation Trust, Southampton, UK.

<sup>3</sup>Estates, University Hospital Southampton NHS Foundation Trust, Southampton, UK.

<sup>4</sup>Department of Infection, University Hospital Southampton NHS Foundation Trust, Southampton, UK.

<sup>5</sup>Clinical and Experimental Sciences, University of Southampton, Southampton, UK.

<sup>6</sup>NIHR Southampton Clinical Research Facility and NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust, Southampton, UK.

## Corresponding author:

Kordo Saeed, Microbiology, Southampton University Hospitals NHS Trust, Tremona Road, Southampton SO16 6YD, UK.

Email: [Kordosaeed@nhs.net](mailto:Kordosaeed@nhs.net)

### Introduction

*Aspergillus spp.* are ubiquitous fungi that commonly occur in soil, water and decaying vegetation. Invasive aspergillosis has been increasingly recognised as a cause of severe illness and mortality in immunocompromised patients (Weber et al., 2009). Patients at risk include those with chronic respiratory conditions such as chronic obstructive pulmonary disease (COPD), haematological and oncological malignancies, HIV and those on immunosuppressive agents. Overall case-fatality rate amongst published reports is as high as 58% (Kanamori, 2015). Most cases of nosocomial aspergillosis are caused by inhalation of fungal spores resulting in invasive pulmonary disease.

*Aspergillus* found inside hospitals usually gains access via ventilation systems, unfiltered air and open windows which allows contamination from recent renovations and construction to reach clinical areas. Other sources include contaminated dust dislodged during hospital renovation, pigeon excreta and food (Richardson and Rautemaa-Richardson, 2019; Weber et al., 2009).

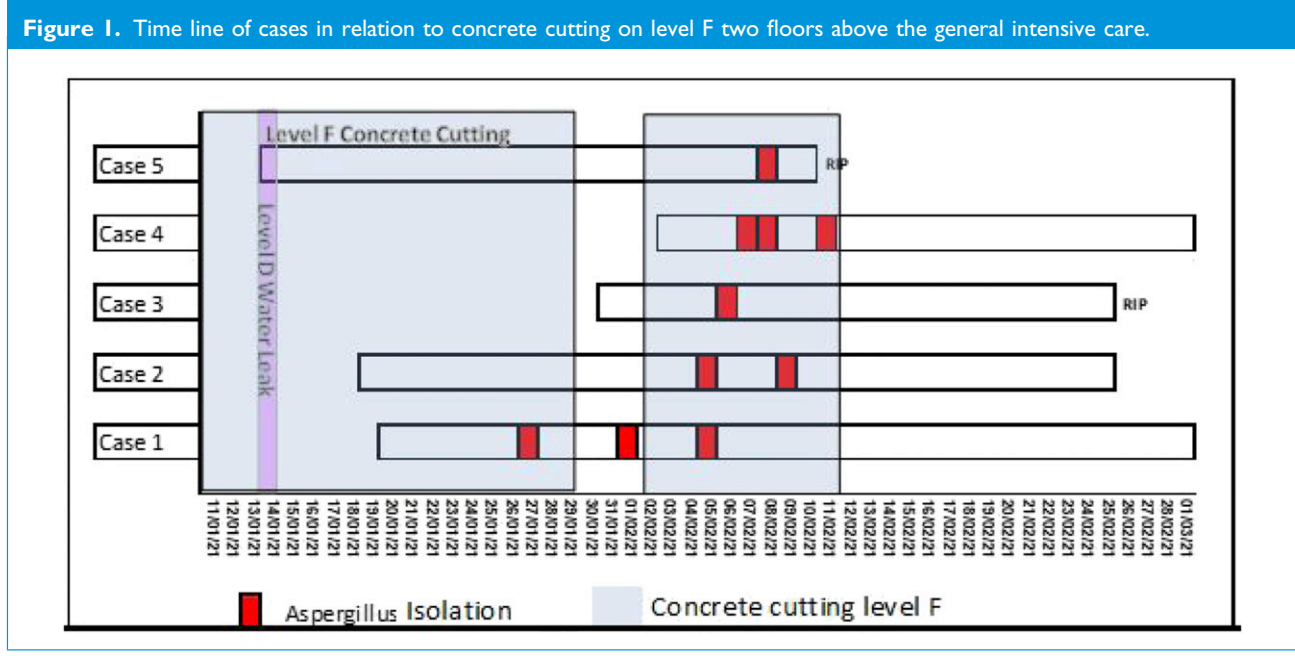
The hospital is a large tertiary teaching hospital with 1194 acute hospital beds and consists of several regional specialist units. In September 2020, it opened its new 22 bedded state of the art general intensive care unit (GICU). The timing of this new unit was coincided with the start of the second wave of the COVID-19 pandemic in the UK. This enabled provision of additional dedicated area for COVID-19 patients including for those transferred from other areas as mutual aid due to lack of ICU beds in regions such as Surrey, Kent and as far away as Birmingham. Being a new unit, the bed spaces and ventilation were compliant with HBN 04-02 and HTM 01-03,

respectively (Department of Health, 2013), meaning we were able to manage two COVID-19 patients in a single bed space. This was part of our preparedness plan based on a risk assessment, for example, where it was deemed not safe to care for critically ill patients outside ICU due to lack of expert staff.

By mid-January 2021, the unit had admitted 95 critically ill patients, and of those 60 patients had SARS-CoV-2 associated respiratory failure. Both the old and the new unit were utilised for all level 3 patients primarily requiring mechanical ventilation, with a 365% increase in the usual capacity. Caring for these patients was supported by staff upskilled from other areas within the hospital. Severe COVID-19 patients with hypoxic respiratory failure often required prolonged periods of prone positioning to optimize oxygenation and a dedicated proning team was supported by members of the local fire service personnel.

On first February 2021, aspergillus was isolated from a routine surveillance respiratory sample from a 64-year-old patient (case 1). This was the index case of aspergillus from our new unit. On sixth February a 64-year-old patient (case 2) had yeast and fungi (later confirmed as aspergillus) identified in their respiratory sample. Both patients had SARS-CoV-2 infection and were mechanically ventilated for severe lung disease. The dedicated GICU microbiologist alerted the GICU intensivists and on further discussion the infection prevention alert level was raised. On the 10th February, a third case was identified (case 3) therefore an outbreak was declared (see Figure 1).

In this report we would like to provide a narrative review of the sequence of events in managing this outbreak during the challenging times of the second SARS-CoV-2 pandemic wave and share our learning with the wider healthcare community.



## Methodology

The new GICU (on level D) has been functional since mid-September of 2020 with an extensive routine microbiological surveillance programme in place for all SARS-CoV-2 patients. This included twice weekly surveillance of respiratory samples in mechanically ventilated patients, most of whom were treated with systemic corticosteroids and/or immunomodulators (e.g. Anti-IL-6 medications) as part of the severe SARS-CoV-2 therapy. There had been no cases of aspergillus since the unit opened or during the previous COVID-19 wave one between April and June 2020. Given that we had three cases of aspergillus in the surveillance samples, a multidisciplinary strategic meeting was arranged for 11th February to investigate and resolve this issue.

The methodology will follow the outbreak process. All relevant parties were invited to an on-line meeting which included microbiologists, infection prevention nurses, intensivists and nursing representatives, domestic services manager, members of the GICU new build project team who were involved in the design and construction of the unit, the hospital estates team and the contracted estates team responsible for the maintenance of GICU.

The meeting explored three main areas

### A) Patients' conditions

There were now three SARS-CoV-2 patients with aspergillus isolated from their respiratory samples. All three were assessed to be clinically immunocompromised due to recent/current high doses of corticosteroid therapy and requiring respiratory support. All three were initially spontaneously ventilating on admission which would have exposed them to a contaminated environment before

requiring invasive mechanical ventilation. While clinically, all three were regarded as colonization, it was challenging to ascertain the clinical significance. Despite the lack of radiological (CT scan) or biochemical (serum Beta-D-glucan) evidence of active invasive infection, all three patients were treated with appropriate antifungal medications (voriconazole). This was decided due to two main reasons. 1) The difficulties in the diagnostic interpretation of abnormal CT scans in patients with severe SARS-CoV-2 infection. 2) The vulnerability of these patients due to the immunocompromised state following treatments with steroids and tocilizumab.

### B) Possible sources of aspergillus

Common sources of aspergillosis infections are the environment and ventilation system. This unit had a new air handling unit providing filtered air at 10 air changes per hour (excluding side rooms). The unit has two distinct sides with doors between areas B and C (see [Figure 2](#)). Although a new theatre suite was being constructed on the floor above, there was no direct access into the unit from this area. All the windows were sealed so contamination from outside was unlikely.

The personal protective clothing (PPE) worn by staff was also considered. Staff wore long sleeve gowns as sessional use and changed their aprons and gloves between patients. Reusable PeRSo hooded respirators were also worn by many staff as they were more comfortable than disposable FFP3 masks ([BAYNHAMS online](#)). Each member of staff was supplied with their own hood, hose, fan and belt and expected to decontaminate and store them appropriately in a dry area after each use. These had been introduced during the first wave of the pandemic. Some members of the proning team were from the fire and rescue service but as

**Figure 2.** General Intensive Care layout, location of water leak, nursing station and cases located on level D.



they were wearing scrubs and full protective clothing it was felt that these were unlikely to be the source of aspergillus.

Another consideration was whether the supplies of equipment and day to day need of clinical items coming into the unit were damp or contaminated.

There was a general discussion about possible water leaks and staining on the ceilings and as a potential source. However, at the end of the meeting a pass away comment was made that there had been a number of water leaks into the unit over the previous month, which would warrant further investigation.

### C) Actions planned

All admitted ICU patients were monitored closely clinically as well as with regular respiratory surveillance (ETA samples) twice weekly. These swabs were taken for surveillance purposes, positive bacterial cultures didn't mean starting a new or changing current antibiotics, all these would have been discussed with a dedicated microbiologist during daily ward round in the GICU. Serum beta-D-Glucan was measured once weekly. It was agreed that if there was a further case, all patients from the same zone (Zone C) would be commenced on appropriate antifungal prophylaxis. During the first meeting a fourth case was reported and consequently all patients were started on antifungal prophylaxis with Posaconazole.

The air handling units on the roof were to be checked to confirm all of the filters had been fitted correctly and that there are no gaps in the ventilation ductwork that would allow contamination in from the surrounding construction areas.

The estates team were to report back on the causes and locations of any water leaks and what actions had been taken at the time.

Settle plates of Sabouraud Dextrose Agar (SAB) were placed at the bed spaces and various locations around the old and the new unit. Routine swabbing of the PeRSO hoods were carried out due to the possibility of aspergillus contamination in storage areas.

## Findings/Results

### A) Patients

Antifungal prophylaxis was to be commenced on patients in GICU if a further case was identified. On 11th February, after the fourth case was confirmed, prophylaxis was commenced on all the patients on the unit because they were on respiratory support and steroids or immunomodulators.

### B) Possible sources: initial findings

Air handling unit filters were inspected. All appeared to be fitted correctly with no bypassing of filters identified.

**Figure 3.** Photograph of settle plate from nurses' station zone C.



However, differential pressure had built up due to dust from ongoing building works so the filters were changed sooner than planned. Swabs from ductwork and filters found no aspergillus.

Around 30 PeRSO hoods were swabbed – no aspergillus isolated from the surveillance swabs. The swabs demonstrated very effective decontamination of the hoods was taking place.

Between the 4th of January and the initial meeting (11 Feb 2021), there had been 3 water leaks into the new unit. One by side room 15 on 08/01/2021, one by the nurses' station on side C on 14/01/2021 and one at the entrance to the unit on 25/01/2021. Three of the patients with aspergillus were in bed spaces close to where the leaks had occurred (see Figure 2).

Two water leaks had been caused by water ingress from the concrete cutting taking place on the floor above in the preceding weeks (Figure 1). The third leak was due to work taking place on the roof and contractors not ensuring the area was adequately weather proofed which allowed rain water to seep down from G level to D level via the construction areas. The contracted estates team had been called to look at the water leaked areas but as the leaks were minimal and had stopped before they arrived, they did not investigate this further other than changing the wet concrete drilling process on the floor above. These leaks were not communicated to the hospital infection prevention team (IPT). Very few members of the estates team had been mask fit tested so little attempt was made to access the unit and to investigate this further.

Thirty settle plates were placed across the whole unit including the old GICU areas. A heavy growth of aspergillus was on the plate at the nurses' station zone C (see Figure 3) and one colony from the plate in bed space 28 where leaks had previously occurred. Penicillium was also isolated from settle plates near to the nurses' station in zone C. This

suggested that the area around the nurse's station in zone C was the potential source of the aspergillus. (see [Figure 2](#))

### Next steps

A decision was taken to investigate the ceiling tiles above the nurse's station in zone C where the water leak had occurred previously. Members of the contracted estates team were mask fit tested so they could enter the COVID-19 area. It was anticipated they would lift a single ceiling tile or use a scope to inspect above the ceiling for any signs of water leak or damp. Unfortunately, contrary to hospital estates advice, the contracted estates staff removed five ceiling tiles exposing a large void at the nurses' station while patients were still in the unit. Fortunately, the patients were not close to the open void. This highlights a gap in understanding of the contracted estates team who were used to working in unoccupied areas. Removal of multiple ceiling tiles should have been carried out in a controlled manner using a plastic 'tube' to reduce the risk of environmental contamination or after patients had been vacated from the area. Pooling water and mould was seen on the ceiling tiles. Water was coming from a small leak at the joint of the domestic hot water pipe. The pipes would have been pressure tested when installed prior to sign off and use in a new building. It is unknown whether this joint was defective or damaged prior to use.

This slow leak meant it had not penetrated through the tile but pooled above the ceiling preventing any immediate awareness. The previous leak had been assumed to be caused by the wet drilling and as there was no investigation above the ceiling tiles this leak was not identified. This was almost directly above the nurses' station where we had highest count from the settle plates ([Figure 3](#)).

Following this finding, all patients were promptly relocated from zone C to zone B to minimise their exposure whilst the works could be carried out. Moving critically ill, mechanically ventilated patients is often difficult and poses additional risk to the patient, but this was deemed necessary to manage the contaminated area effectively. This was logistically challenging but possible because we had seen a reduction in SARS-CoV-2 cases and had available surge capacity. Removal of ceiling tiles further exposes the patients, staff and environment to aspergillus and other organisms. All equipment moved out from zone C and were decontaminated if possible or discarded if deemed necessary.

The ceiling tiles were removed, bagged and swabbed prior to disposal. As wet/damp areas may provide an environment for aspergillus to flourish, all wet lagging around the pipes were removed and thorough checks were made to ensure that no wet or damp material remained. Once the works were completed, the whole area had a deep clean using a hypochlorite to remove residual organisms.

Once deep cleaning was completed the patients were moved back into zone C which enabled estates staff to

inspect zone B more closely, where a previous leak had also occurred. No ongoing issues were identified on zone B.

Swabs from the ceiling tiles in zone C resulted in a confluent growth of *Penicillium* and *Aspergillus* ([Figure 4](#)).

### Impact on patients

Following epidemiological review three patients were included in the outbreak. Duty of Candour was observed for all the patients. Two patients were never placed within the new unit – zone B and C. The fourth case was a mutual aid patient transferred from an ICU outside our region from Surrey and was always intubated and on closed circuit ventilation. Hence, it is unlikely that the case was exposed to the environment locally. Case five was a poly trauma patient (not SARS-CoV-2) who was cared for in a different part of the unit. The patient was a builder and it was assessed their aspergillus was probably from their accident on a building site. Two out of the three patients included in the outbreak subsequently died, but on root cause analysis and clinical reviews neither death was due to aspergillus infections. University Hospital Southampton (UHS) GICU death rate for COVID-19 was 26.9%, well below the national average of 36.5% meaning UHS had one of the top performing ICUs in the UK ([Dushianthan et al., 2022](#)).

All isolates were sensitive to Posaconazole and Voriconazole which was used for prophylaxis and pre-emptive treatment.

### Discussion

There have been several reports of COVID-19-associated pulmonary aspergillosis (CAPA), raising concerns about this superinfection as an additional contributing factor to mortality and there are consensus guidance for research and clinical management ([Koehler et al., 2021](#); [van Arkel et al., 2020](#)).

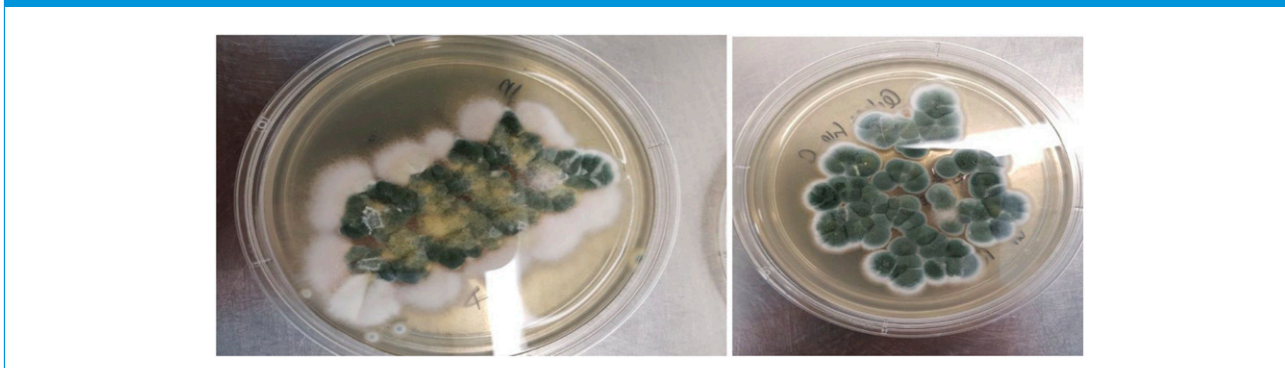
Additionally while there are a number of report on outbreaks of aspergillosis in the intensive care ([Demuyser et al., 2019](#)). To our knowledge, there are no reports on how to manage potential aspergillus outbreaks in the ICU among COVID-19 cases. Comparisons between the ones involved non-COVID-19 cases with us is challenging, especially as most patients with COVID-19 were given high dose steroids and/or immunomodulators in the ICU.

This report highlights the importance of surveillance, early escalation of unusual findings and communication in preventing and managing outbreaks especially those related to buildings, leaks and estates; our four C (Clinical, Control of Infection, Communication and Continuous education) key learnings are summarised in ([Table 1](#))

### Outcome

There was no long term impact on any of the patients. No patient was denied access to level 3 care whilst zone C was

**Figure 4.** Photographs of cultures from swabs of the wet ceiling tile in zone C.



**Table 1.** A summary of four C key learnings (Clinical, Control of Infection, Communication and Continuous education).

Category of learning	What we learnt
Clinical	Routine surveillance is essential to promptly identify clusters that require further investigation. This is particularly important when dealing with a large number of cases from an emerging infection like SARS-CoV-2
	Once the cause of the problem is identified, adequate clinical treatment and or prophylaxis should be instigated
	Maintain patient safety and when appropriate relocation of patients from high-risk areas when an environmental contamination is identified. In this case 13 patients were moved out of GICU zone C, this, although safely performed, was a major logistical issue and should be included in future contingency plans
	Consider impact on laboratory, for example, additional diagnostics
Control of infection	Consider impact on pharmacy and antimicrobial stewardship programme: In this case additional antifungal usage
	All water leaks must be reported to infection prevention team and fully investigated. Even if the visible dripping has stopped there may be residual issues which needs to be addressed
	Important to consider estate and environmental factors not just clinical practice when investigating an outbreak
Communication	Consider ongoing quality assurances regarding the state of estates
	Inform the infection prevention team about leaks in clinical areas particularly where immunocompromised patients are managed
	Multidisciplinary outbreak meetings means a diversity of issues both clinical and non-clinical can be discussed and considered when looking for the source or cause of an outbreak
Continuous education	Consider duty of candour to patients/relatives
	Lack of understanding of the consequences of water leaks should be highlighted to staff including colleagues from estates
	The importance of infection control when removing ceiling tiles should be highlighted to staff and estate teams and this should be carried out in a controlled way
	Few estates staff assessed by occupational health as able to work in a high-risk area
	Mask fit testing of hospital staff including estates staff

closed. Fortunately, the incident occurred after the peak of admissions and the large bed spaces meant patients could be doubled up to enable remedial works to take place. On risk assessment this was deemed necessary to prevent further exposure to aspergillus spored and provide care for these patients within critical care footprint with well-trained staff.

Both the contracted and hospital estates team have undergone training and education about how to investigate and manage water and sewage leaks to ensure there are no ongoing consequences to patients or staff. The Infection Prevention Team are also raising awareness amongst clinical staff about the possible consequences of a water leak and that patients need to be moved out of an area when

ceiling tiles are being removed and works are required to take place.

Since the fixing of the slow leak there have been no further cases of aspergillus colonisations or infections within the new GICU.

## Conclusion

This outbreak clearly demonstrated that water leaks must be fully investigated to ensure the actual cause has been identified and rectified and all remedial works have been carried out. The estates team made the assumption all the water leaks were due to the contracted works on the floors above. Lack of available fit tested staff meant a reluctance to enter GICU and investigate 'in person'. The assumption was made the water had stopped dripping, the contractors above had changed their wet drilling practice, therefore the problem was resolved. No attempt was made to remove wet or damp items including ceiling tiles.

Using the diverse knowledge and expertise of the people present at the outbreak meeting, meant environmental and clinical aspects were suggested, discussed and investigated. Settle plates identified specifically where the source of the aspergillus was, focusing activity to one small area within a large and complex unit.

This outbreak was identified promptly and pro-actively managed despite this taking place during the second wave of the pandemic when the focus could have been solely on SARS-CoV-2 meaning other outbreaks could have been missed. The excellent team work within the hospital meant once the issue was identified it could be rapidly rectified to restore essential GICU capacity.

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## ORCID iD

Kordo Saeed  <https://orcid.org/0000-0003-0123-0302>

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