



## SARS CoV 2 and Coronaviridae in Children: An Updated Review

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### Abstract

**Background:** With more than 800000 deaths and 20 million of confirmed cases worldwide, SARS-CoV 2 is one of the worst pandemic of the last decade. Questions concern the etiology of this pandemic outbreak. Was the world prepared for this pandemic? Efforts have been oriented towards treating patients who are infected presenting severe Covid-19 and preventing the spread of the virus by several means [lockdown, quarantine, social distancing, masks, antiseptic solutions]. Whereas evidence concerning the etiology treatment is still uncertain and lacking at this moment, efforts in developing vaccines for preventing another future pandemic are organized. What lessons can we get from this pandemic? Several papers have reported that children present less severe signs and symptoms than adults. There is also evidence that children at any age can be severely affected. If children are less affected than adults, why is it so? With this serious pandemic outbreak, were we or will we be prepared in the future to face a similar serious worldwide health emergency? How will we be prepared?

The Objectives of this review was to find answers to the above mentioned questions.

**Methods and Materials:** This review was realized between 18 March 2020 and 30 June 2020 by electronic search of scientific articles dealing with Covid-19 or SARS-CoV 2 or Coronaviridae in children in Google and Pubmed databases without date limitation. 1085 articles were identified among which 200 were retained for analysis and 48 were included for the review.

**Results and Conclusions:** Several reviews have been published today. This review brings updates on the outbreak of the SARS-CoV 2 pandemic in children.

**Keywords:** Covid-19; SARS-Cov 2; Pandemic; Coronaviridae; Children; Review

### Introduction

Since December 2019, the world has been facing a global health emergency situation caused by the COVID-19 (coronavirus disease 2019) pandemic outbreak. According to the World Health Organization (WHO) coronavirus disease situation reports of 20 August 2020, there were 22 566 220 confirmed cases and 782456 deaths worldwide with the Americas being the most affected continent (11 887 224 confirmed cases) followed by Europe (3 874 604 confirmed cases), South East Asia (3 308 987 confirmed cases), Eastern Mediterranean (1 776 899 confirmed cases), Africa (975 551 confirmed cases) and Western Pacific (432 214 confirmed cases) [1].

In almost 2 decades, there have been three pandemic outbreaks caused by coronaviruses [2-5]. The first coronavirus outbreak epidemic took place in 2002-2003 in China and Hong Kong which was caused by unknown coronavirus identified as SARS-CoV (severe acute respiratory syndrome coronavirus) responsible of 8422 cases and 916 deaths [2-5]. The second epidemic outbreak occurred in 2012 in the Middle East, in Saudi Arabia where the identified etiologic coronavirus was MERS-CoV [Middle East respiratory syndrome coronavirus] which caused 2495 cases and 858 deaths [2]. The third pandemic outbreak began in December 2019 in Wuhan, China and has affected the whole world with the known worldwide dramatic health, social and economic consequences; the pathogen

rapidly identified was SARS-CoV 2 (severe acute respiratory syndrome coronavirus 2), another coronavirus [4,6,7]. If this evolution continues, one would expect another pandemic outbreak caused by another unknown pathogen and more virulent agent to occur within a decade or earlier. What lessons can we get from these repetitive pandemic outbreaks?

What explains this dramatic evolution with successive pandemic outbreaks?

Coronaviruses are crownlike viruses which cause seasonal common colds in children and adults in general [8]. Several pathogenic and more virulent strains have emerged namely SARS-CoV, MERS-CoV and SARS-CoV 2 which cause more than common colds precisely pneumonia and severe acute respiratory syndrome. Coronaviruses are part of the coronaviridae family [9,10]. These viruses have an RNA [ribonucleic acid] genome. The coronaviridae are divided in four subgroups alpha, beta, gamma and delta coronaviruses [9,10]. The subgroup alpha coronavirus contains 11 subtypes among which are human CoV 229E, Bat CoV 1A. The subgroup beta contains 17 subtypes among which are SARS-CoV, MERS-CoV and SARS-CoV2. In the subgroups delta and gamma there are 7 and 2 subtypes respectively. Each subtype of each subgroup can present different strains which highlight the complexity of these viruses [9]. Alpha and beta coronaviruses infect mammals, delta and gamma coronaviruses infect avian species and mammals [9,10]. Reservoir hosts are bats and rodents for alpha and beta coronaviruses. Reservoir hosts for delta and gamma coronaviruses are unknown [10]. Camels are known reservoir hosts for MERS-CoV. Pangolins are suspected intermediate reservoir hosts for SARS-CoV [9].

SARS-CoV 2 has a genome which resembles to SARS-like bat CoV by more than 80%. SARS-CoV and SARS-CoV2 have 73% similarity in receptor binding domains [9]. SARS-CoV 2 spike glycoprotein (which is the part of the virus interacting with the angiotensin converting enzyme receptor at the surface of cells to enter the latter) is a combination of bat SARS-CoV and a non identified beta coronavirus [9].

The mortality rate of SARS-CoV, MERS-CoV and SARS-CoV2 is 10, 37 and 2% respectively. Compared to SARS-CoV and MERS-CoV, SARS-CoV 2 is more contagious with a transmission rate (R0) of 2-3 [9].

Transmission is between individuals by direct contact, aerosolization, airborne and contact with infected surfaces [11,12].

Since the beginning of the pandemic, a lot of scientific publications have emerged concerning SARS-CoV 2 and COVID-19. The physiopathology of severe acute respiratory syndrome due to SARS-CoV 2 has been widely explored and is beginning to be elucidated [4]. A lot of published papers reported higher susceptibility to COVID-19 in high risk adult patients compared to children [4]. Children were considered to be less affected than adults by COVID-19 however several severe cases reporting Kawasaki-like syndrome rapidly emerged during the pandemic in Europe [13]. This review had the objective of updating data concerning COVID-19 in children since the beginning of the pandemic in December 2019 and also to determine how the situation has been dealt with and evolved from a local point of view to a global point of view.

## Methods and Materials

Electronic search of Google and Pubmed databases was realized between 18 March and 30 June 2020 for articles dealing with Covid-19 or SARS-CoV 2 or coronaviridae in children in Google and Pubmed databases without date limitation. 1085 articles were identified among which 200 were retained for analysis of which 48 were included for the review.

## Results

The articles included were mainly reviews, case series, case reports, observational prospective and retrospective studies and experience sharing point of views.

In the general population, children present 1-5% of the infected cases [14]. In the general pediatric population, the infected cases with SARS-CoV 2 represent between 0.02 and 12,3% [15,16]. In the general population, 5-10% of the infected individuals develop complete severe respiratory syndrome in COVID-19 and the majority of the infected cases develop mild to moderate respiratory symptoms [17]. 7.8% of the pediatric cases develop severe COVID-19 [15]. All ages are susceptible of being affected from neonates to teenagers [18-22]. Mortality rate of COVID-19 is between 2-3% [20]. The proportion of asymptomatic pediatric patients varies between 15 and 50% [16,23-26]. Most of the infected children (more than 90%) present as asymptomatic or with mild to moderate symptoms and signs [27]. Common symptoms and signs reported in children were fever, cough, sore throat, flu-like syndrome, pneumonia, abdominal pain, vomiting, diarrhea; neurologic symptoms and signs like axial hypotonia, drowsiness and moaning sounds [16,20,26-31].

On laboratory findings, increase in c-reactive protein, procalcitonin and lactate dehydrogenase can be observed [20].

Several cases of Kawasaki-like syndromes have been reported in Europe since the outbreak of the pandemic [13,32,33]. This clinical presentation is due to a post viral immunological reaction to SARS-CoV 2 [13]. In a case series, it has been reported fatal outcome in rare cases of Kawasaki-like syndrome [32]. Treatment with intravenous immunoglobulins and corticosteroids improved outcome in Kawasaki-like syndrome [13].

As in adults, the severe and critical deterioration observed in SARS-CoV 2 infected patients has the same etiopathology in children, namely cytokine storm which is a hyperinflammatory state characterized by an increased release of different cytokines. The increase in cytokine release is responsible of organ failure which can be observed in severely and critically affected patients with SARS-CoV2 [4,34-38].

SARS-CoV 2 has a transmissibility rate ( $R_0$ ) of 2-3 and is higher than that of SARS-CoV or MERS-CoV [22]. The transmission is interindividual, perinatal with possible vertical transmission, airborne, by aerosolization and by contact with infected surfaces [11,18,19,39-41].

The median incubation period is 4.7 days (3-7) [3]. However there is evidence that that this period could be longer than 14 days [29,42].

Diagnosis can be made by detecting viral RNA with real-time reverse transcriptase PCR [polymerase chain reaction] assay on pharyngeal swabs or stool swabs bearing in mind that confirmed cases of SARS-CoV 2 on pharyngeal swabs can reveal positive stool swabs during the convalescent period after negativation of the respiratory swabs up to 14 days later. This observation may indicate a possible oro-fecal transmission [43].

CT thoracic scans may help to confirm the diagnosis in confirmed and suspected cases. Most common

imaging findings on thoracic CT scans were bilateral patchy ground glass opacities [16].

CT scans should be used with caution in children in order to avoid unnecessary radiation.

Treatment is mainly symptomatic and supportive in severe cases including mechanical ventilation and cardiocirculatory support [44].

Several therapeutics used in COVID-19 in adults have not showed their efficacy in terms of survival. In children, these drugs have not been studied in large pediatric cohorts and will not be discussed here.

Vaccines could be a solution for preventing a new pandemic outbreak. To date there are no approved human coronavirus vaccines. SARS-CoV and MERS-CoV vaccines have been tested in animals but did not reach the phase I and thus cannot be tested in humans. Vaccines for SARS-CoV 2 need safety evaluation in humans and this can take some time. Antibodies in coronavirus infections are not always related to a long-lived immunity and reinfection is possible in some individuals with mild symptoms or no symptoms [8]. The future vaccines have to take this observation into account. In SARS-CoV 2 the target for vaccine has been identified as the surface protein S [8].

Several groups are working on vaccines using protein subunit, RNA, DNA, non replicating vector, inactivated virus, attenuated virus and virus-like particle based vaccine candidates [8]. Vaccine development takes time because of the necessity to go through different clinical research phases which may take up to 18 months or more. The muting characteristics of coronaviruses could explain the difficulties and challenges in the development of vaccines. The ideal vaccine would be the one that would protect against all coronaviruses. The muting characteristics of coronaviridae is also a threat of future epidemics and pandemics. This underlines the importance of developing polyvalent vaccines [8].

The best treatment remains prevention and in the absence of a vaccine, usual preventive measures including quarantine in confirmed or suspected cases, antiseptic solutions and masks remain applicable and have shown their efficacy.

## Discussion

Since the outbreak of COVID-19 pandemic in December 2019. Several measures have been decided worldwide to reduce and stop the spread including lockdowns, social distancing, quarantine, masks and antiseptic solutions. Local and global functioning had to be reorganized in hospitals to face the increasing number of pa-

tients admitted to hospitals and the intensive care units. In France, the Paris Hospitals, Assistance Publique Hôpitaux de Paris (APHP) had to reorganize and centralize the management of hospital admissions in order to cope with this health emergency and deal with the increasing number of admissions [13,45]. Necker Enfants Malades University Hospital is the referential Center for SARS-CoV 2 pediatric patients in Paris.

At the beginning of the pandemic outbreak, there were no severe or critically ill pediatric patients admitted for SARS-CoV 2 in Necker Enfants Malades University Hospital. Later on several cases concerning a recrudescence of Kawasaki-like syndrome were reported. In Necker Enfants Malades University Hospital several dozens of children with suspected and confirmed Kawasaki-like syndrome were admitted with favorable outcome after intravenous immunoglobulins and corticosteroids [13]. The increase of this pediatric vasculitis was related to SARS-CoV 2 exposure in these children. This pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV2 infection is a state of post-viral immunological reaction to SARS-CoV-2 [13]. In this clinical presentation of COVID 19, superantigens could be involved by inducing a hyperinflammatory state with increase of cytokine release responsible of a multisystem inflammatory response syndrome in children. This observation confirms that children can also be severely impacted by SARS-CoV 2. Other coronaviruses have been reported to cause Kawasaki-like and Kawasaki syndromes.

Several publications have reported that children were less susceptible to SARS-CoV 2. Hypotheses explaining why children seem less impacted by SARS-CoV include different activity in the expression of angiotensin converting enzyme 2 receptor which plays a role in virus cell entry; a more developed innate immune system developed in children; immunosenescence due to aging in adults; the presence of other viruses in pediatric respiratory tract limits the development of SARS-CoV 2; children travel less and thus less exposed; immature immune system and weaker adaptative immune response in children limiting the hyperinflammation.

Apart from being affected physically, the SARS-CoV 2 pandemic outbreak has also revealed that children were particularly mentally and psychologically affected as revealed in a recent survey [6]. Another consequence of this pandemic is the risk and possibility of increasing learning gaps in most vulnerable children due to school closure [46]. School closure has proved it's efficacy in reducing the

number of infected cases as well. A modelling study to predict the number of COVID-19 infected pediatric patients to be admitted to hospital and in the pediatric intensive care unit in the USA before end 2020 has been published [47].

According to this modelling study using a cumulative pediatric infection proportion scenario of 5%, there would be 3.7 million of children infected with SARS-CoV 2, 9907 severely ill children requiring hospitalization and 1086 critically ill children requiring pediatric intensive care unit (PICU) in the USA [47]. This study underlines the importance of anticipating the propagation of the epidemic in order to apply the preventive measures and also prepare the hospitals to face epidemic emergency health states. Similar modelling scenarios have been employed in France in Paris Hospitals, Assistance Publique Hôpitaux de Paris (APHP) to face the pandemic [45]. These scenarios also can help to prepare the outbreak of a second pandemic wave in the actual period which remains a possible challenging eventuality. What explains the emergence of a such global and worldwide public health crisis? A possible hypothesis of this worldwide spreading of the epidemic can be explained by the travelling and social mixing lifestyles which underline the importance and basis of lockdowns to prevent the spread of the virus. A recent paper reporting the analysis of the genome of SARS-Cov 2 strains in infected cases diagnosed in the beginning of the epidemic in France revealed that the actual epidemic outbreak in France and Europe was not caused by initial imported cases from Wuhan but caused by strains of unknown origin [48]. This observation could indicate other possible etiologies of the origin of the pandemic namely changes in the ecosystem with possible mutations of existing coronaviruses becoming more pathogen and virulent. SARS-CoV2 has a lot of similarities with SARS-CoV and Bat SARS-CoV [9]. Bats are known reservoir hosts and pangolins as intermediate hosts for SARS-CoV. There are probably more other unknown coronavirus reservoirs which constitute a potential source of emerging virulent pathogens. This emphasizes the urgent necessity of developing polyvalent vaccines against existing virulent coronaviruses and also capable of neutralizing potential emerging muting strains of coronaviridae.

## Conclusion

Most coronaviruses cause common colds in children with flu-like syndrome clinical presentation. The latest identified coronaviruses SARS-CoV, MERS-CoV and SARS-CoV2 can cause severe acute

respiratory syndrome less commonly in children of all ages. In this critical and severe clinical presentation, patients can present with multiple organ failure which is due to an exacerbated immunologic reaction with increased cytokine and other inflammation mediators release characteristic of cytokine storm.

In children, a particular severe clinical presentation has been described and reported, namely Kawasaki-like syndrome which is due to an immunologic reaction involving superantigens after exposure to SARS-CoV 2. Favorable outcome with corticosteroids and passive immunization therapy with intravenous immunoglobulins has been described in children with Kawasaki-like syndrome.

Barrier protective measures remain the most effective prevention to date in the absence of an available vaccine against SARS-CoV2 and other potential pathogenic and virulent coronaviruses. Coronaviridae have some identified reservoir hosts but there are still other non identified potential reservoir hosts which may constitute a possible source of other emerging viruses which could cause new pandemic outbreaks. This implies a continuous preparedness in order to control future pandemic outbreaks. Preparedness necessitates a close collaboration of the scientific research community, healthcare givers and the main stakeholders at a global level. Vaccines are solutions to prevent new pandemics. Due to the mutating characteristics of coronaviridae, a polyvalent vaccine capable of neutralizing different coronaviruses might be a future promising solution. In the meantime, a vaccine against SARS-CoV 2, responsible of the actual pandemic outbreak is an urgent priority to control the spread of the disease.

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## Conflict of Interest

None.

## Bibliography

1. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports>
2. Singhal T. "A Review of Coronavirus Disease-2019". *The Indian Journal of Pediatrics* 87.4 (2020): 281-286.
3. Lai CC., et al. "Asymptomatic Carrier State, Acute Respiratory Disease and Pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-Cov 2): Facts and Myths". *Journal of Microbiology, Immunology and Infection* 53.3 (2020): 404-412.
4. Haslak F, et al. "Childhood Rheumatic Disease and Covid-19 Pandemic: An Intriguing linkage and a New Horizon". *Balkan Medical Journal* 37.4 (2020): 184-188.
5. Guarner J. "Three emerging coronaviruses in two decades. The story of SARS, MERS and Now COVID -19". *American Journal of Clinical Pathology* 153 (2020): 420-421.
6. Jiao WY., et al. "Behavioral and Emotional Disorders in Children during the COVID-19 Epidemic". *European Paediatric Association* 221 (2020): 264-266.
7. Kickbusch I., et al. "COVID-19: How a virus is turning the world upside down". *BMJ* 369 (2020): m1336.
8. Amanat F and Krammer F. "SARS-CoV 2 Vaccine: Status Report". *Immunity* 52 (2020): 583-589.
9. Shereen MA., et al. "COVID-19 infection: Origin, Transmission and Characteristics of Human Coronaviruses". *Journal of Advanced Research* 24 (2020): 91-98.
10. Abd El-Aziz TM and Stockand JD. "Recent Progress and Challenges in Drug Development Against COVID-19 Coronavirus (SARS-CoV 2)- An Update in the Status". *Genetics and Evolution* (2020).
11. Cao Q., et al. "SARS-CoV 2 infection in Children: Transmission dynamics and clinical characteristics". *Journal of Formosan Medical Association* 119 (2020): 670-673.
12. Xu Y. "Unveiling the origin and transmission of 2019-nCoV". *Trends in Microbiology* 28.4 (2020): 239-240.
13. Toubiana J., et al. "Kawasaki-like Multisystem Inflammatory Syndrome in Children During The Covid-19 Pandemic in Paris, France: Prospective Observational Study". *BMJ* 369 (2020): m2094.
14. Ludvigsson J. "Systematic Review of COVID 19 in Children shows milder cases and a better prognosis than adults". *Acta Paediatrica* (2020): 1-8.
15. She J., et al. "COVID-19 epidemic: Disease Characteristics in Children". *Journal of Medical Virology* (2020): 1-8.
16. Lu X., et al. "SARS-CoV 2 infection in children". *The New England Journal of Medicine* 382 (2020): 1663-1665.
17. Ceccarelli M., et al. "Difference and similarities between severe acute respiratory syndrome (SARS)-Coronavirus (CoV) and SARS-CoV 2. Would a rose by another name smell as sweet?" *European Review For Medical and Pharmacological Sciences* 24 (2020): 2781-2783.

18. Sun D., *et al.* "Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: A single Center Observational Study". *World Journal of Pediatrics* (2020).
19. Canarutto D., *et al.* "COVID-19 infection in a paucisymptomatic infant; raising the index of suspicion in epidemic settings". *Pediatric Pulmonology* (2020): 1-2.
20. Morand A., *et al.* "COVID-19 virus and children: what do we know?" *Archives de Pédiatrie* 27 (2020): 117-118.
21. Chen Y., *et al.* "Infants Born to Mothers with a new coronavirus (COVID 19)". *Frontiers in Pediatrics* 8 (2020): 104.
22. Zeng L., *et al.* "Neonatal Early-Onset Infection with SARS-CoV 2 in 33 neonates born to mothers with COVID in Wuhan, China". *JAMA Pediatrics* 174.7 (2020): 722-725.
23. Qiu H., *et al.* "Clinical and Epidemiological Features of 36 Children With Coronavirus disease 2019 (COVID-19) in Zhejiang, China. An Observational Cohort Study". *Lancet Infection Disease* 20 (2020): 689-696.
24. Hagmann SHF. "COVID-19 in children: More than meets the eye". *Travel Medicine and Infectious Disease* (2020).
25. Yonker LM., *et al.* "Lessons unfolding from pediatric cases of COVID-19 disease caused by SARS -CoV 2 infection". *Pediatric Pulmonology* 55.5 (2020): 1085-1086.
26. Su L., *et al.* "The different clinical characteristics of coronavirus disease cases between children and their families in China-The Character of Children with COVID-19". *Emerging Microbes and Infections* 9 (2020).
27. Dong Y., *et al.* *Pediatrics* 145.6 (2020): e20200702.
28. Nathan N., *et al.* "Atypical Presentation of COVID -19 in young Infants". *Lancet* 395.10235 (2020): 1481.
29. Zheng F., *et al.* "Clinical Characteristics of Children with Coronavirus Disease 2019 in Hubei China". *Current Medical Science* 40.2 (2020): 1-6.
30. Hong H., *et al.* "Clinical Characteristics of novel coronavirus disease 2019 in newborns, infants and children". *Pediatrics and Neonatology* (2020).
31. Lu Q and Shi Y. "Coronavirus disease (COVID-19) and neonate: what neonatologists need to know". *Journal of Medical Virology* (2020): 1-4.
32. Riphagen S., *et al.* "Hyperinflammatory Shock in Children during COVID-19 Pandemic". *Lancet* 395.10237 (2020): 1607-1608.
33. Esper F., *et al.* "Association between a Novel Human Coronavirus and Kawasaki Disease". *The Journal of Infectious Diseases* 191.4 (2005): 499-502.
34. Radbd J., *et al.* "Use of Tocilizumab for COVID-19 infection induced cytokine release syndrome :A Cautionary Case Report". *Chest* (2020).
35. Xu X., *et al.* "Effective treatment of severe COVID-19 patients with Tocilizumab". *Proceedings of the National Academy of Sciences of the United States of America* 117.20 (2020): 10970-10975.
36. Zhang S., *et al.* "Rationale use of Tocilizumab in the treatment of novel coronavirus pneumonia". *Clinical Drug Investigation* (2020).
37. Jamilloux Y., *et al.* "Should we stimulate or suppress immune responses in COVID -19 ? Cytokine and anti-cytokine intervention". *Autoimmunity Reviews* (2020).
38. Ye Q., *et al.* "The pathogenesis and treatment of cytokine storm in COVID-19". *Journal of Infection* (2020).
39. Jogalekar MP., *et al.* "Novel 2019 Coronavirus: Genome Structure, Clinical Trials and Outstanding Questions". *Experimental Biology and Medicine* (2020): 1-6.
40. Xu Y., *et al.* "Characteristics of Pediatric SARS-CoV 2 infection and potential evidence for persistent fecal viral shedding". *Nature Medicine* 26 (2020): 502-505.
41. Gagneur A., *et al.* "Vertical Transmission of human coronavirus. Prospective pilot study". *Pathologie Biologie* 55 (2007): 525-530.
42. Lin J., *et al.* "The isolation period should be longer: lesson from a child infected with SARS-CoV 2 in Chongqing, China". *Pediatric Pulmonology* (2020): 1-4.
43. Zhang T., *et al.* "Detectable SARS-CoV 2 viral RNA in feces of three children during recovery period of COVID -19 pneumonia". *Journal of Medical Virology* 92.7 (2020): 909-914.
44. Hong X., *et al.* "Extracorporeal membrane oxygenation (ECMO): does it have a role in the treatment of severe COVID-19?" *International Journal of Infectious Disease* 94 (2020): 78-80.
45. The COVID-19-APHP Group. "Assistance Publique Hôpitaux de Paris Response to The COVID-19 Pandemic". *Lancet* (2020).
46. Van Lancker W and Parolin Z. "COVID-19, school closures, and child poverty: a social crisis in the making". *Lancet* 5.5 (2020): e243-e244.

47. Pathak EB., *et al.* "COVID-19 in children in the United States: Intensive Care Admissions, Estimated Total Infected, and Projected Numbers of Severe Pediatric Cases in 2020". *Journal of Public Health Management and Practice* 26.4 (2020): 325-333.
48. Gambaro F., *et al.* "Introduction and early spread of SARS-Cov 2 in France". *bioRxiv* (2020).

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