# Biosafety and action in front of COVID-19: What do we know?

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## Abstract:

*The COVID-19 disease that affected the entire world in 2020 is caused by a virus (SARS-CoV-2) with a high rate of pathogenicity and transmission that caused several deaths in its trajectory. To combat this disease several personal hygiene measures and the use of personal protective equipment were necessary. In view of this, the study aims to clarify some doubts regarding the vaccine and its effectiveness, individual protection and the performance of health professionals in the face of this situation.*

**Keywords:** Biosafety, SARS-CoV-2, Cross Infection, Health Professionals, COVID-19, Personal Protective Equipment (PPE).

## 1. Introduction

COVID-19 or SARS-CoV-2 is an infection caused by viruses with a high rate of transmission and pathogenicity (SHEREEN et al., 2020). This virus has been known since 2003 under the name of SARS-CoV, however its mutation has been spread around the world still with a doubtful fuse (SHEREEN et al., 2020)

The spread of the virus was very fast, and in a matter of time it was already at the pandemic level (SHEREEN et al., 2020). In view of this, habits had to be enhanced and Personal Protective Equipment used rigorously (ROTHAN; BYRAREDDY, 2020) to avoid cross-infection being just one of the many necessary means in opposition to COVID-19 (ROTHAN; BYRAREDDY, 2020).

The World Health Organization (WHO) has created a set of rules in the fourth edition of the biosafety manual to be applied to the pathogen that is the protagonist of the pandemic (HUI, 2017). According to the WHO (WHO, 2020) several means of combating SARS-CoV-2 and controlling acute respiratory infections are plausible, such as constant hand hygiene, use of 70% gel alcohol and N95 medical

mask or with disposable upper protection (WORLD HEALTH ORGANIZATION (WHO), 2020) . It is of utmost importance the need for adequate disinfectants with proven activity against enveloped viruses, such as the use of hypochlorite, quaternary ammonia compounds and alcohol (WORLD HEALTH ORGANIZATION, 2020a).

Health biosafety laboratories must maintain all appropriate practices and tests for COVID-19 must be carried out in laboratories properly equipped with trained technicians (HUI, 2017).

The present work, based on the information presented, aimed at bibliographic survey of the safety condition achieved from prevention and risk control actions inherent to activities that compromise human health and personal protective equipment (PPE) used by health professionals and its relevance in tackling the COVID-19 pandemic.

## 2. Materials and methods

This work was produced by reviewing the literature on the Google Scholar, PubMed and SciELO databases, and had as its central theme: “Biosafety and action in front de COVID-19: What do we know”, in the following subdivisions: “Biosafety, laboratory tests cross-infection ”,“ Review of the action of health professionals in the fight against COVID-19”,“Myths about early treatment ”,“Covid-19 and perspectives for the future ”and“ Vaccine and our salvation ”. In addition, searches were performed using the keywords such as: “Cross Infection COVID-19”, “Biosafety and SARS-CoV-2”, “Health Professionals”, “COVID-19” and “Personal Protection Equipment (PPE)”.

The articles were based on descriptors created by the Virtual Health Library developed (http://decs.bvs.br/homepage.htm) from MeSH - Medical SubjectHeadings of the US National Library of Medicine (NLM), which allows terminology in common in Portuguese, English and Spanish.

These search methods led to data from articles by the World Health Organization (WHO). The inclusion criteria for the articles selected for the present research were: articles published in magazines and newspapers indexed in the databases mentioned above; Articles published in the English language; Articles published in the period from 2014 to 2021.

## 2. Results and discussion

From a literature review with 60 articles, 45 were selected in order to inform and reaffirm health professionals about the importance of using personal protective equipment and the risks of SARS-CoV-2 transmission to the population.

*2.1 Laboratory tests and cross-infection*

According to the WHO (WHO, 2020), means of combating SARS-CoV-2 are essential and they are: constant hand hygiene, use of 70% gel alcohol and N95 medical mask or with disposable upper protection, facial protection as faceshield and gloves (AĞALAR; ÖZTÜRK ENGIN, 2020; JOAQUIM et al., 2020).

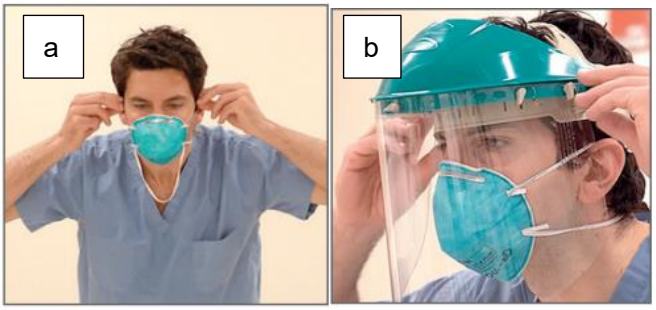


**Figure 1:** a - Removal of the medical mask by the elastics avoiding contamination; b - Removal of the faceshield (ORTEGA et al., 2020).

According to the World Health Organization (WHO), biosafety laboratories are a strategic approach to managing risks to human health and ensuring that health laboratories comply with appropriate biosafety practices against the spread of COVID-19 (WORLD HEALTH ORGANIZATION, 2020b). All tests with clinical samples from patients to check for the presence of SARS-CoV-2 must be carried out in properly equipped laboratories (WORLD HEALTH ORGANIZATION, 2020b), with a team trained in the techniques and safety of procedures.

The most effective test recommended by the World Health Organization is the RT-PCR (PEELING et al., 2020), which comes from the English Reverse-transcriptase polymerase chain reaction (RT-PCR) and is an exam considered standard in the diagnosis of COVID-19 (CADARI et al., 2021). In this, the evidence of the SARS-CoV-2 RNA in the sample analyzed in the nasopharyngeal swab scraping (CORMAN et al., 2020) occurs by the reverse transcription polymerase chain reaction (STRUNK et al., 2014).

Given the need for close contact between healthcare professionals and infected patients to obtain nasopharyngeal or oropharyngeal samples, the possibility of self-collection of saliva will significantly decrease the chance of transmission of COVID-19. In addition, this collection is not comfortable and can cause bleeding , especially in patients with thrombocytopenia (BAGHIZADEH FINI, 2020). Chest Computed Tomography (CT), as a routine imaging tool for diagnosing pneumonia, is relatively easy to perform and can produce a quick diagnosis. In this context, chest CT can provide benefits for the diagnosis of COVID-19 (STRUNK et al., 2014).

The laboratory guidelines on biosafety must be followed in all circumstances to avoid the spread of the virus that has such a high and rapid rate of transmission (WORLD HEALTH ORGANIZATION, 2020b). Laboratories that do not submit to the biosafety recommendations must transfer the samples to national, regional or international reference laboratories with the SARS-CoV-2 detection capacity in force in the biosafety pre-established in the fourth edition of the laboratory's biosafety manual (HUI, 2017).

According to an article published in "*The Lancet Infectious Diseases*", serology tests are recommended for rapid screening of symptomatic individuals from COVID-19 in community settings, without much access to the molecular test (PEELING et al., 2020). A positive result for IgM in symptomatic patients is strongly suggestive of SARS-CoV-2 infection. According to the same authors, this approach is probably more effective in individuals 5 to 10 days after the onset of symptoms. However, it is not recommended for population methodologies in low prevalence environments, as it generates more false-

positive results compared to true-positives leading to a false sense of security regarding immunity in the population, leading to premature easing of public health measures based on misleading disease estimates (PEELING et al., 2020).

In clinical environments, such as hospitals and dental clinics, some standards must be followed to avoid cross-infection and spread of the new coronavirus (MENG; HUA; BIAN, 2020) and according to the same authors, all environments, in general, must follow the steps of dressing, wearing protective masks against the dissipation of droplets and hand hygiene in order to avoid possible contamination (MENG; HUA; BIAN, 2020).

According to the initial view of the United Kingdom's National Health Service (NHS), dentists and their staff should continue to provide routine care for asymptomatic patients with no history of close contact and to discourage symptomatic patients from attending. However many general dentists have reduced routine care so as not to spread COVID-19 among their patients given the social distance measures that were introduced to the population by the British government (COULTHARD, 2020).

Soon after, some recommendations for dental practice were made to prevent and control infections: dentists should take strict personal protection measures and avoid or minimize operations that may produce droplets or aerosols. The four-handed technique is beneficial for controlling infection; the use of low or high volume saliva ejectors can reduce the production of drops and aerosols (MENG; HUA; BIAN, 2020).

At the moment, vaccination is already active in several countries ((THANH LE et al., 2020), but it is still essential to detect diseases early and immediately isolate the infected person from the healthy population (STRUNK et al., 2014).

Cases of early death from the COVID-19 outbreak occurred mainly in the elderly, possibly due to a weak immune system that allows a faster progression of viral infection (ROTHAN; BYRAREDDY, 2020). Diagnostic accuracy can be improved by combining clinical evidence with chest computed tomography (CT) and RT-PCR results, and RT-PCR results should be interpreted according to epidemiological, clinical and radiological factors (PASCARELLA et al., 2020).

*2.2 Review of the action of health professionals in the fight against COVID-19*

The pandemic is causing a lot of stress in health professionals, due to many different reasons, such as the severity of the infection, the easy spread, the lack of knowledge about the virus, the depletion of personal protective equipment, lack of access to updated information and communication, the shortage of ventilators and beds in the intensive care unit (EL-HAGE et al., 2020; GEORGER et al., 2020). In addition, given the mode of transmission in the virus, exposure to body fluids (saliva, blood, among others) and high amount of aerosol production, as is the case especially with dentists, leave them exposed to a high risk of infection by SARS-CoV-2 (ALI; RAJA, 2020; GE et al., 2020).

Studies have shown that health professionals in general today have satisfactory knowledge on the subject, and those who keep up to date on the virus are more likely to be aware of protective measures during patient care (BHAGAVATHULA et al., 2021; DALKY et al., 2021; MODI et al., 2020).

To solve these problems, the routine in offices and hospitals has changed. For infection control, each patient should be managed as if he were infected, thus carrying out preventive measures (gloves, aprons, goggles, face shields and masks such as N95)(AMATO et al., 2020; IZZETTI et al., 2020; MENG; HUA; BIAN, 2020). Studies have reported that the virus can persist on surfaces for a few days, especially

those suspended in human secretions (KAMPF et al., 2020; KRAMER; SCHWEBKE; KAMPF, 2006; OTTER et al., 2013), so surface disinfection is indispensable not for work environments. Other alternatives were also suggested, such as conducting anamnesis remotely, measuring the temperature when arriving at an office and avoiding companions during an appointment (AMATO et al., 2020)

*2.3 Myths about early treatment*

Many stem cell studies have shown positive results against the serious symptoms of COVID-19 disease (LOURENÇO et al., 2020). Meanwhile, chloroquine, which is an antimalarial agent with anti-inflammatory and immunomodulatory activities, has gained greater interest as a potential therapeutic option for the management of COVID-19 (KLIETZ et al., 2019). In early February of the year 2020, Wang and associated researchers (WANG et al., 2020) demonstrated in vitro chloroquine activity against SARS-CoV-2 and these findings led to support for the clinical use of chloroquine in China during this outbreak. Although the rationale for this pharmacological dosing regimen remained unclear, it was announced in mid-February that promising initial results have been demonstrated (KLIETZ et al., 2019) and numerous national governors have begun disclosure.

However, on March 28, 2020, there were more than 21 clinical trials underway registered and 3 prophylactic studies evaluating the effectiveness of hydroxychloroquine (HCQ) for the treatment of SARS-Cov-2 (MADEWELL et al., 2020). Of those studies that reported more detailed results and received significant media attention. This way HCQ was proposed in higher doses than those used to treat autoimmune disorders and together with azithromycin (AZM), a macrolide antibiotic (ROSENBERG et al., 2020). However, many authors criticized the study due to the lack of low power, limited follow-up, confusion by indication and lack of adherence to the allocated treatment arm (MADEWELL et al., 2020). The effectiveness of HCQ in combination with AZM, therefore, has not yet been established, but approval of compassionate use by regulators and media attention is likely to lead to an increase in the use of this combination therapy for the treatment of COVID-19 worldwide (MADEWELL et al., 2020).

In the year 2020, the safety profile of hydroxychloroquine was described in its summary, the characteristics of the products, with adverse reactions to drugs, including severe cardiac disorders, such as prolongation of the QT segment (QT represents the repolarization of the ventricular action potentials that is controlled by several ion channels) that can lead to arrhythmia, myocardial arrest or cardiovascular death (MADEWELL et al., 2020; ROSENBERG et al., 2020). In a study by Mahévas (MAHÉVAS et al., 2020) concluded that HCQ did not significantly reduce admission to the ICU or ARDS in patients hospitalized with hypoxemic pneumonia due to COVID-19. In that same study, the authors stated that the results are of great importance and do not support the use of HCQ in patients hospitalized for documented SARS-CoV-2 pneumonia (MAHÉVAS et al., 2020).

Even with all these uncertainties about early treatment, the president of the current moment, persisted in encouraging the population and publicizing in media the use of these drugs that are known to induce cardiotoxicity when used alone, and also increase the risk of other drugs that prolong the QTc (corrected QT) interval (LU et al., 2015). Therefore, it is of utmost importance to understand the safety implications of the proposed combination of HCQ and AZM before this becomes standard practice in the

management of COVID-19 globally since many studies have been terminated due to drug toxicity (MAGAGNOLI et al., 2020)

In a survey (BRUM ELIANE, [s.d.]) it was revealed that the Brazilian president had executed an institutional strategy for the spread of the corona virus. The Center for Research and Studies on Health Law (CEPEDISA) of the Faculty of Public Health (FSP) of the University of São Paulo (USP) and Connects Human Rights since March of the previous year were dedicated to investigating the federal and state rules regarding the new corona virus. From this, a bulletin entitled "*Rights in Pandemic - Mapping and Analysis of Legal Norms in Response to Covid-19 in Brazil*" was produced. According to the same (BRUM ELIANE, [s.d.]) a special edition was recently launched where the research stated the existence of an institutional strategy for the spread of the virus, promoted by the Brazilian Government under the leadership of the Presidency of the Republic.

In addition to positions coming from the national regent not consistent with the national biosafety rule such as inappropriate use of a mask and stimulating agglomeration, the president also, according to the news, becomes explicit against which populations the attacks are concentrated on. According to the report, there are a series of measures taken by the president to prevent workers from protecting themselves from covid-19 and isolating them (BRUM ELIANE, [s.d.]).

Another drug that was suggested against COVID-19 was Ivermectin (JEAN; HSUEH, 2020). However, according to the same authors, the dosage for an action to fight the virus is very high, and the results were only clinical. The proposed dosage for its inhibitory action for SARS-CoV-2 is often toxic, the maximum accepted and according to the same article, to date, no specific medication or therapy against SARS-CoV-2 is formally recommended by the Food and Drug Administration (FDA) in the United States of America (EUA) (JEAN; HSUEH, 2020). In Brazil, due to an excessive use and proposed by the current Brazilian government of 2021, the news "*Ivermectin, like the Bolsonaro government, is not effective against COVID-19*" reinforces that the measured and researchers have said of the action of the medicine against parasites but not for infections caused by the new virus (SAKAMOTO, [s.d.]). In addition, the drug is also leaving sequelae, since several cases of patients with liver cirrhosis are being reported by the medical community due to the chronic use of Ivermectin (NUNES, [s.d.]).

### *2.4 Covid-19 and prospects for the future*

RNA viruses, such as SARS-CoV-2, have high mutation rates, which can increase virulence and pathogenicity of the virus (ABDULLAHI et al., 2020). A major concern in this regard are mutations in the protein Spike (S), responsible for binding the virus to host cells (GURUPRASAD, 2021; ROBSON, 2020).

The coronavirus can become weaker or stronger with time and, as demonstrated in a study, there is a theoretical possibility that in the future the virus will cause milder or more serious effects (NAGY; PONGOR; GYŐRFFY, 2021). According to the same authors, mutations that mild signs and symptoms can facilitate the spread of the virus and thus maintain the outbreak. The mutations that generate a more serious disease, on the other hand, need to be monitored and studied on an emergency basis to avoid further impasses.

With the increase in the number of infected people around the world, the likelihood of new mutations that are successful and cause problems in the effectiveness of already approved vaccines is more

likely (ABDULLAHI et al., 2020). As an example, a new variant of COVID-19, P.1, found in Brazil, in the state of Manaus may reduce the ability of antibodies to neutralize the action of the virus, according to an observation made by the World Health Organization (WHO), being necessary to prove this fact (SILVA, [s.d.]). Therefore, it is once again evident the importance of complying with social isolation, adopting biosafety measures and also promoting and disseminating vaccination as soon as possible before it loses/decreases its effectiveness.

*2.5 Vaccine and our salvation*

The vaccine is part of a major advance in science, having an impact on longevity and human health (PLOTKIN, 2014). It exposes beings to very small and safe amounts of attenuated substances or dead viruses and bacteria and works by inferring immune responses that are proven to protect against repeated natural infections (PLOTKIN; GILBERT, 2012). It was Pasteur who most clearly formulated the idea of attenuation and demonstrated its usefulness, first with Pasteurella multocida, the cause of a diarrheal disease in chickens (PLOTKIN, 2014). His first approaches involved exposure to oxygen or heat, which played a role in the development of the rabies vaccine and in the famous anthrax challenge experiment in Pouilly-le-Fort (PLOTKIN, 2005).

However, the most powerful technique of serial multiplication of a pathogen in vitro or in usual hosts originated with Calmette and Guérin, who passed bovine tuberculosis bacteria 230 times artificially to obtain an attenuated strain for protection against human tuberculosis (MARTIN, 2006). Later in the 20th century, Sellards and Laigret (LAIGRET, 2005) and, more successfully, Theiler and Smith attenuated the yellow fever virus by serially passing through mice and chicken embryo tissues, respectively.

When you are exposed, the immune system will learn to recognize, attack infections and during the process of developing immunity, the body produces antibodies against specific microorganisms and creates defense (DAI et al., 2019). The next time a person encounters this microorganism, the antibody prevents them from causing the disease or alleviates the severity of the disease, regardless of how the vaccine is made. There are currently four different types of vaccines designed to boost your immune system and prevent serious and fatal diseases (DAI et al., 2019). Live attenuated vaccines contain a version of the live virus that has been weakened so as not to cause serious illness in people with a healthy immune system, such as the yellow wound vaccine. Another common method of vaccine production is the inactivation of the pathogen by heat or chemical treatment, for example hepatitis A (BAXTER, 2007). Subunit, recombinant, polysaccharide and conjugate vaccines are Biosynthetic vaccines that contain artificial substances that are very similar to fragments of viruses or bacteria, the hepatitis B vaccine is an example. Toxoid vaccines are made up of selected toxins that have been sufficiently attenuated and are capable of inducing a humoral immune response such as against tetanus (BAXTER, 2007).

In Brazil, according to the report "*4 vaccines against Covid present satisfactory rates of efficacy and safety; see comparative*", the vaccines that are in circulation are two vaccines: CoronaVac, developed by the Sinovac laboratory in partnership with the Butantan Institute, and the Oxford vaccine, developed by AstraZeneca and the University of Oxford, in partnership with the Oswaldo Cruz Foundation (Fiocruz) (MODELLI, [s.d.]).


**Figure 2:** Vaccine from the Butantan Institute and Chinese pharmaceutical company Sinovac thrown in BBC News Brazil news (PASSARINHO, [s.d.])

The vaccine will be made available to everyone free of charge by the Unified Health System (SUS), according to the report "*Vaccination against Covid-19 in Brazil: see questions and answers*" which shows several questions that have occurred (POR PORTAL G1, [s.d.]). Vaccination will follow a sequence of priority that, according to the national immunization plan, the campaign's priorities are: people aged 60 or more institutionalized, people with institutionalized disabilities, indigenous peoples living on indigenous lands, health workers, people aged 60 or over more, traditional riverside peoples and communities, traditional quilombola peoples and communities, people with comorbidities, people with severe permanent disabilities, people on the street, population deprived of liberty, employee of the deprivation of liberty system, education workers; Security, Rescue and Armed Forces; Public road passenger transport workers; metro and rail transport workers; air transport workers; waterway transport workers; truckers; port workers and industrial workers (POR PORTAL G1, [s.d.]).

The same reported that in São Paulo soon after the approval of the emergency use of Anvisa, on January 17 began vaccination and on January 18, another fifteen states began to vaccinate the population.


**Figure 3:** First vaccinated in the country, nurse Mônica Calazans, 54, receiving the first dose of the CoronaVac vaccine against Covid-19 at Hospital das Clínicas, in São Paulo, Photo: Amanda Perobelli / Reuters.

Even the same virtual newspaper emphasizes that it is not possible to contract COVID-19 after vaccination, since no vaccine in tests contains the live virus, therefore, it is impossible for you to be infected when vaccinated (POR PORTAL G1, [s.d.])

## 3. Conclusion

In this study, we were able to conclude that biosafety is of extreme importance, both for health professionals and patients. In addition, a major step towards science was the vaccine and, being the only cure for the corona virus, its use and its dissemination as soon as possible is extremely important, in an attempt to prevent further mutations from the virus. It is also concluded that dental surgeons, due to the nature of their profession, are subject to high risks of infection, which implies an increased attention of these professionals.

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## 5. References

ABDULLAHI, I. N.; EMERIBE, A. U.; AJAYI, O. A.; ODERINDE, B. S.; AMADU, D. O.; OSUJI, A. I. Implications of SARS-CoV-2 genetic diversity and mutations on pathogenicity of the COVID-19 and biomedical interventions. **Journal of Taibah University Medical Sciences**, [s. l.], v. 15, n. 4, p. 258–264, 2020.

AĞALAR, C.; ÖZTÜRK ENGIN, D. **Protective measures for covid-19 for healthcare providers and laboratory personnel**, 2020.

ALI, K.; RAJA, M. Coronavirus disease 2019 (COVID-19): challenges and management of aerosol-generating procedures in dentistry. **Evidence-Based Dentistry**, [s. l.], v. 21, n. 2, p. 44–45, 2020.

AMATO, A.; CAGGIANO, M.; AMATO, M.; MOCCIA, G.; CAPUNZO, M.; DE CARO, F. Infection Control in Dental Practice During the COVID-19 Pandemic. **International Journal of Environmental Research and Public Health**, [s. l.], v. 17, n. 13, p. 4769, 2020.

BAGHIZADEH FINI, M. **What dentists need to know about COVID-19**, 2020.

BAXTER, D. **Active and passive immunity, vaccine types, excipients and licensing**. Occupational Medicine, [s. l.], v. 57, n. 8, p. 552–556, 2007.

BHAGAVATHULA, A. S.; RAGHAVAN, V. R.; AHMADI, A.; SRIRAG, D.; CHATTU, V. K. Frontline Healthcare Workers' Knowledge, Perception and Risk Prevention Practices Regarding COVID-19 in Afghanistan: A Cross-Sectional Study. **Medical Sciences**, [s. l.], v. 9, n. 1, p. 2, 2021.

BRUM ELIANE, E. B. Pesquisa revela que Bolsonaro executou uma "estratégia institucional de propagação do coronavírus". **EL PAÍS**, [s. l.], [s.d.].

CADARI, M. B.; CACHONI, A. C.; TOLEDO NETO, J. L.; JASSI JOSÉ, F.; ZORZI COLÉTE, J.; FOGGIATO, A. A.; DA SILVA, D. F. **Biosafety, life and COVID-19: Online questionnaire**. International Journal of Advanced Engineering Research and Science, [s. l.], v. 8, n. 1, p. 059–068, 2021.

CORMAN, V. M.; LANDT, O.; KAISER, M.; MOLENKAMP, R.; MEIJER, A.; CHU, D. K. W.; BLEICKER, T.; BRÜNINK, S.; SCHNEIDER, J.; SCHMIDT, M. L.; MULDERS, D. G. J. C.; HAAGMANS, B. L.; VAN DER VEER, B.; VAN DEN BRINK, S.; WIJSMAN, L.; GODERSKI, G.; ROMETTE, J. L.; ELLIS, J.; ZAMBON, M.; PEIRIS, M.; GOOSSENS, H.; REUSKEN, C.; KOOPMANS,

M. P. G.; DROSTEN, C. **Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR.** Eurosurveillance, [s. l.], v. 25, n. 3, p. 1–8, 2020.

COULTHARD, P. **Dentistry and coronavirus (COVID-19) - moral decision-making.** British Dental Journal, [s. l.], 2020.

DAI, X.; XIONG, Y.; LI, N.; JIAN, C. Vaccine Types. **Vaccines - the History and Future**, [s. l.], p. 1–9, 2019.

DALKY, H. F.; GHADER, N.; AL KUWARI, M.; ALNAJAR, M.; ISMAILE, S.; ALMALIK, M.; SHUDIFAT, R.; SANAD, S.; AL-NSAIR, N.; AL MATROOSHI, F. Assessment of the Awareness, Perception, Attitudes, and Preparedness of Health-care Professionals Potentially Exposed to COVID-19 in the United Arab Emirates. **Journal of Multidisciplinary Healthcare**, [s. l.], v. Volume 14, p. 91–102, 2021.

EL-HAGE, W.; HINGRAY, C.; LEMOGNE, C.; YRONDI, A.; BRUNAULT, P.; BIENVENU, T.; ETAIN, B.; PAQUET, C.; GOHIER, B.; BENNABI, D.; BIRMES, P.; SAUVAGET, A.; FAKRA, E.; PRIETO, N.; BULTEAU, S.; VIDAILHET, P.; CAMUS, V.; LEBOYER, M.; KREBS, M.-O.; AOUIZERATE, B. **Health professionals facing the coronavirus disease 2019 (COVID-19) pandemic: What are the mental health risks?** L'Encéphale, [s. l.], v. 46, n. 3, p. S73–S80, 2020.

GE, Z.; YANG, L.; XIA, J.; FU, X.; ZHANG, Y. P**ossible aerosol transmission of COVID-19 and special precautions in dentistry**. Journal of Zhejiang University-SCIENCE B, [s. l.], v. 21, n. 5, p. 361–368, 2020.

GEORGER, F.; DOS SANTOS, E.; GAZAGNE, L.; BERDAGUÉ, P.; SAIB, A.; NAHON, S.; PIQUET, J.; AMARA, W. COV IMPACT : analyse des différents facteurs de stress du personnel hospitalier dans 2 centres hospitaliers en France lors de la pandémie COVID-19. **Annales de Cardiologie et d'Angéiologie**, [s. l.], v. 69, n. 5, p. 227–232, 2020.

GURUPRASAD, L. Human SARS CoV-2 spike protein mutations. **Proteins: Structure, Function, and Bioinformatics**, [s. l.], p. prot.26042, 2021.

HUI, D. S. **Epidemic and Emerging Coronaviruses (Severe Acute Respiratory Syndrome and Middle East Respiratory Syndrome)**. Clinics in chest medicine, [s. l.], v. 38, n. 1, p. 71–86, 2017.

IZZETTI, R.; NISI, M.; GABRIELE, M.; GRAZIANI, F. COVID-19 **Transmission in Dental Practice: Brief Review of Preventive Measures in Italy**. Journal of Dental Research, [s. l.], v. 99, n. 9, p. 1030–1038, 2020.

JEAN, S. S.; HSUEH, P. R. Old and re-purposed drugs for the treatment of COVID-19. **Expert Review of Anti-Infective Therapy**, [s. l.], v. 18, n. 9, p. 843–847, 2020.

JOAQUIM, B. F.; TOLEDO NETO, J. L.; COLÉTE, J. Z.; FOGGIATO, A. A.; SILVA, D. F. **Dentistry biosecurity during the SARS-CoV-2 pandemic: what should we know?** Joaquim,. [s. l.], p. 1–45, 2020.

KAMPF, G.; TODT, D.; PFAENDER, S.; STEINMANN, E. **Persistence of coronaviruses on inanimate surfaces and their inactivation with biocidal agents**. Journal of Hospital Infection, [s. l.], v. 104, n. 3, p. 246–251, 2020.

KLIETZ, M.-L.; KAISER, H. W.; MACHENS, H.-G.; AITZETMÜLLER, M. M. Ac c ep te d Corresponding Author : an us cr ip t Ac c ep te d us cr t. [s. l.], p. 1–31, 2019.

KRAMER, A.; SCHWEBKE, I.; KAMPF, G. H**ow long do nosocomial pathogens persist on inanimate surfaces? A systematic review.** BMC Infectious Diseases, [s. l.], v. 6, n. 1, p. 130, 2006.

LAIGRET, J. La petite histoire de la découverte de la vaccination contre la fièvre jaune - Jean Laigret (1893-1966). **Medecine tropicale : revue du Corps de sante colonial**, [s. l.], v. 65, n. 3, p. 290–292, 2005.

LOURENÇO, O. D.; JASSI, F. J.; COLÉTE, J. Z.; FOGGIATO, A. A.; TOLEDO NETO, J. L.; SILVA, D. F. STEM CELLS IN THE TREATMENT OF COVID-19 ACUTE RESPIRATORY SYNDROME: What do we know so far ? [s. l.], v. 10, p. 43079–43083, 2020.

LU, Z. K.; YUAN, J.; LI, M.; SUTTON, S. S.; RAO, G. A.; JACOB, S.; BENNETT, C. L. **Cardiac risks associated with antibiotics: Azithromycin and levofloxacin**, 2015.

MADEWELL, Z. J.; YANG, Y.; JR, I. M. L.; HALLORAN, M. E.; DEAN, N. E. NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice. 1. **medRxiv**, [s. l.], p. 1–13, 2020.

MAGAGNOLI, J.; NARENDRAN, S.; PEREIRA, F.; CUMMINGS, T.; HARDIN, J. W.; SUTTON, S. S.; AMBATI, J. **Outcomes of hydroxychloroquine usage in United States veterans hospitalized with Covid-19.** medRxiv, [s. l.], 2020.

MAHÉVAS, M.; TRAN, V. T.; ROUMIER, M.; CHABROL, A.; PAULE, R.; GUILLAUD, C.; GALLIEN, S.; LEPEULE, R.; SZWEBEL, T. A.; LESCURE, X.; SCHLEMMER, F.; MATIGNON, M.; KHELLAF, M.; CRICKX, E.; TERRIER, B.; MORBIEU, C.; LEGENDRE, P.; DANG, J.; SCHOINDRE, Y.; PAWLOTSKI, J. M.; MICHEL, M.; PERRODEAU, E.; CARLIER, N.; ROCHE, N.; DE LASTOURS, V.; MOUTHON, L.; AUDUREAU, E.; RAVAUD, P.; GODEAU, B.; COSTEDOAT-CHALUMEAU, N. **No evidence of clinical efficacy of hydroxychloroquine in patients hospitalised for COVID-19 infection and requiring oxygen: Results of a study using routinely collected data to emulate a target trial**. medRxiv, [s. l.], p. 1–20, 2020.

MARTIN, C. **Tuberculosis vaccines: Past, present and future.** Current Opinion in Pulmonary Medicine, [s. l.], v. 12, n. 3, p. 186–191, 2006.

MENG, L.; HUA, F.; BIAN, Z. **Coronavirus Disease 2019 (COVID-19): Emerging and Future Challenges for Dental and Oral Medicine**. Journal of Dental Research, [s. l.], v. 99, n. 5, p. 481–487, 2020.

MODELLI, L. **4 vacinas contra a Covid apresentam taxas satisfatórias de eficácia e de segurança; veja comparativo**. [s.d.].

MODI, P. D.; NAIR, G.; UPPE, A.; MODI, J.; TUPPEKAR, B.; GHARPURE, A. S.; LANGADE, D. COVID-19 Awareness Among Healthcare Students and Professionals in Mumbai Metropolitan Region: A Questionnaire-Based Survey. **Cureus**, [s. l.], 2020.

NAGY, Á.; PONGOR, S.; GYŐRFFY, B. Different mutations in SARS-CoV-2 associate with severe and mild outcome. **International Journal of Antimicrobial Agents**, [s. l.], v. 57, n. 2, p. 106272, 2021.

NUNES, K. Ineficaz contra a Covid-19, ivermectina tem aumento de 615% nas vendas em Pernambuco. **Brasil de fato - pernanbuco**, [s. l.], [s.d.].

ORTEGA, R.; GONZALEZ, M.; NOZARI, A.; CANELLI, R. **Personal Protective Equipment and Covid-19**. New England Journal of Medicine, [s. l.], 2020.

OTTER, J. A.; YEZLI, S.; SALKELD, J. A. G.; FRENCH, G. L. **Evidence that contaminated surfaces contribute to the transmission of hospital pathogens and an overview of strategies to address contaminated surfaces in hospital settings**. American Journal of Infection Control, [s. l.], v. 41, n. 5, p. S6–S11, 2013.

PASCARELLA, G.; STRUMIA, A.; PILIEGO, C.; BRUNO, F.; DEL BUONO, R.; COSTA, F.; SCARLATA, S.; AGRÒ, F. E. **COVID-19 diagnosis and management: a comprehensive review**, 2020.

PASSARINHO, N. **A potencial vantagem da CoronaVac contra variantes do coronavírus**. [s.d.].

PEELING, R. W.; WEDDERBURN, C. J.; GARCIA, P. J.; BOERAS, D.; FONGWEN, N.; NKENGASONG, J.; SALL, A.; TANURI, A.; HEYMANN, D. L. **Serology testing in the COVID-19 pandemic response**. The Lancet Infectious Diseases, [s. l.], v. 20, n. 9, p. e245–e249, 2020.

PLOTKIN, S. **History of vaccination**, 2014.

PLOTKIN, S. A. **Vaccines: Past, present and future**. Nature Medicine, [s. l.], v. 11, n. 4S, p. S5, 2005.

PLOTKIN, S. A.; GILBERT, P. B. Nomenclature for immune correlates of protection after vaccination. **Clinical Infectious Diseases**, [s. l.], 2012.

POR PORTAL G1. Vacinação contra a Covid-19 no Brasil: veja perguntas e respostas. [s. l.], [s.d.].

ROBSON, B. COVID-19 Coronavirus spike protein analysis for synthetic vaccines, a peptidomimetic

antagonist, and therapeutic drugs, and analysis of a proposed achilles' heel conserved region to minimize probability of escape mutations and drug resistance. **Computers in Biology and Medicine**, [s. l.], v. 121, p. 103749, 2020.

ROSENBERG, E. S.; DUFORT, E. M.; UDO, T.; WILBERSCHIED, L. A.; KUMAR, J.; TESORIERO, J.; WEINBERG, P.; KIRKWOOD, J.; MUSE, A.; DEHOVITZ, J.; BLOG, D. S.; HUTTON, B.; HOLTGRAVE, D. R.; ZUCKER, H. A. **Association of Treatment with Hydroxychloroquine or Azithromycin with In-Hospital Mortality in Patients with COVID-19 in New York State.** JAMA - Journal of the American Medical Association, [s. l.], 2020.

ROTHAN, H. A.; BYRAREDDY, S. N. **The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak**, 2020.

SAKAMOTO, L. S. **Ivermectina, como o governo Bolsonaro, não tem eficácia contra a covid-19.** [s.d.].

SHEREEN, M. A.; KHAN, S.; KAZMI, A.; BASHIR, N.; SIDDIQUE, R. **COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses**. Journal of Advanced Research, [s. l.], v. 24, p. 91–98, 2020.

SILVA, L. B. **Covid-19: Cepa de Manaus pode comprometer desenvolvimento de anticorpos, diz OMS**. [s.d.]. Disponível em: <https://www.cnnbrasil.com.br/saude/2021/02/10/covid-19-cepa-de-manaus-pode-comprometer-desenvolvimento-de-anticorpos-diz-oms>.

STRUNK, J. L.; TEMESGEN, H.; ANDERSEN, H.; PACKALEN, P. In Pr es s In es. [s. l.], v. 80, n. 2, p. 1–8, 2014.

THANH LE, T.; ANDREADAKIS, Z.; KUMAR, A.; GÓMEZ ROMÁN, R.; TOLLEFSEN, S.; SAVILLE, M.; MAYHEW, S. **The COVID-19 vaccine development landscape.** Nature reviews. Drug discovery, [s. l.], v. 19, n. 5, p. 305–306, 2020. Disponível em: <http://dx.doi.org/10.1038/d41573-020-00073-5>

WANG, P. W.; LU, W. H.; KO, N. Y.; CHEN, Y. L.; LI, D. J.; CHANG, Y. P.; YEN, C. F. **COVID-19-Related Information Sources and the Relationship with Confidence in People Coping with COVID-19: Facebook Survey Study in Taiwan**, 2020.

WHO. Rational use of personal protective equipment for coronavirus disease 2019 ( COVID-19 ). **World Health Organization**, [s. l.], v. 27, n. February, p. 1–7, 2020.

WORLD HEALTH ORGANIZATION. Laboratory biosafety guidance related to coronavirus disease (COVID-19). **Interim guidance**, [s. l.], n. 19 March, p. 1–5, 2020. a.

WORLD HEALTH ORGANIZATION. Laboratory biosafety guidance related to the novel coronavirus ( 2019-nCoV ). **World Health Organisation**, [s. l.], n. February, p. 1–12, 2020. b.

WORLD HEALTH ORGANIZATION (WHO). Rational use of personal protective equipment for coronavirus disease 2019 ( COVID-19 ). **World Health Organization**, [s. l.], 2020.