Hypotheses: implementation of Le Chatelier's principle as a potential integrative method to prevent and or cure coronavirus

Jawad Alzeer[1,2]^, Fawzi Al-Razem[2]

[1]Halalopathy, Swiss Scientific Society for Developing Countries, Zurich, Switzerland; [2]College of Medicine and Health Sciences, Palestine Polytechnic University, Hebron, Palestine

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Correspondence to: Jawad Alzeer. Halalopathy, Swiss Scientific Society for Developing Countries, Zurich, Switzerland; College of Medicine and Health Sciences, Palestine Polytechnic University, Hebron, Palestine. Email: jawad.alzeer@chem.uzh.ch.

Abstract: The COVID-19 is an infectious disease caused by a newly discovered coronavirus (SARS-CoV-2) and is mainly considered a respiratory tract illness, even though it may influence other body functions. The virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes. The number of infected people and deaths associated with COVID-19 is increasing on a daily basis and the current third wave of the pandemic appears to be worse than the one that swept several countries over the summer. The only aspect that can be reasonably managed in this pandemic is the environmental stress, which is important to boost the patient's immune system and the patient's ability to recover. Here we propose a potential integrative method to prevent and or attempting to cure coronavirus patients using safe and available resources that can be administered easily by most patients. This treatment is taking advantage of the equilibrium Law as explained by Le Chatelier principle and implemented through the use of antiseptics/disinfectants that can be administered by inhalation without harming the patient's health. This proposed method is expected to reduce the COVID-19 virus load to a threshold that could boost the patient's immune system and speed recovery.

Keywords: COVID-19; SARS-CoV-2; environment stress; disinfectant; concentration gradients; bicarbonate

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Introduction

The number of people infected with the new coronavirus continues to increase; by mid-December 2020, there were approximately 75 million people infected and 1.6 million death worldwide. Health management, control, and/or treatment of COVID-19 coronavirus disease is limited (1). Classically, the general method of inactivating viruses is either through macromolecules such as vaccines, which have the potential to block receptors and ultimately block the viral activity or through micromolecules, where the RNA sequence could be selectively targeted and block processes essential for viral replication. Fortunately, two vaccines have been approved, short term safety is promising, but long-term safety remain an open question (2). Vaccine for COVID-19 is prophylactic, taken for prevention not for cure. For this reason, COVID-19 treatment must be investigated and implemented quickly to contain the global spread of the virus and make it easily available worldwide.

^ ORCID: 0000-0002-1447-4683.

One option was well evaluated, based on the treatment of the symptoms associated with the viral infection. For this reason, hydroxychloroquine (3) and remdesivir (4) were introduced as potential drugs to cope with the viral symptoms. Both drugs will neither cure the coronavirus nor limit its spread, but the two drugs and others could potentially contribute to a more tolerable progression of the virus. Currently, there is a consensus among scientists that the best available option is still to activate the patient's immune system. The response of the immune system varies according to age, state of health, and environmental stress. In a pandemic situation, age and patient's health cannot be managed, while environmental stress can be manipulated more effectively to stimulate the immune response. Patients infected with coronaviruses are under great mental and physical stress, therefore it is necessary to create favorable circumstances that can cope with the environmental stress (5). Mental stress can be managed by specialists, whereas physical stress, which is the most important, can only be managed by physical means.

In this context, we propose a new hypothesis, based on the principle of Le Chatelier to reduce the coronaviruses to a threshold that could boost the immune system (6) and allow the patient to better cope with the infection. The method could conceivably be used as an adjunct therapy, with potential to be effective, environmentally friendly, easily accessible, and convenient to protect patients from coronaviruses and most likely from other viral infections.

Hypothesis

In general, the dose determines the toxicity. In the case of coronavirus, this means that when the infectious dose is increased, the probability of infection and illness is likely to increase. For this reason, wearing a mask is recommended. When an infected person moves without a mask, the virus particles begin to move in the same direction, with relatively few microscopic states. As the intensity increases, the potential energy of the virus increases, initiating a coordinated action of particles that cause the virus to turn into aggressive particles that can infect and spread infection to others. While the mask dispersing virus particles lead to a non-concerted action, the movement of particles became uncoordinated, random in all directions, with many microscopic states. The increasing disorder of the virus particles, resulting from dispersion and subsequent dilution of the particles in the atmosphere, reduces their potential and makes the virus less effective (7).

It is generally believed that reducing the infectious dose of COVID-19 could reduce its infectious potential and lead to less severe cases (8). The high infectious dose is associated with a higher viral load and thus higher disease progression and transmission. The virus spreads from person to person primarily through saliva droplets or discharge from the nose when an infected person coughs or sneezes. The risk of infection is likely to be significant only if a minimal infectious dose is developed or viral loads reach thresholds for transmission (9). This concept led us to propose a new hypothesis based on a dose-dependent response and dispersion attitude, in which an individual with a high infectious dose is likely to develop severe COVID-19 symptoms and transmit infection to others. Droplet transmission requires close contact between susceptible and infectious individuals, and the more a virus has replicated in the body, as a consequence, the higher the viral load, which in turn is likely to be a strong determinant of transmission risk. This perspective led us to propose that the intensity of coronaviruses in the patient's body (inside) and in the patient's surroundings (outside) is at a constant ratio. As the intensity of the virus within the infected person increases, the intensity around the infected person likewise increases. Similarly, when the intensity inside decreases, the intensity outside decreases. We therefore propose that if the intensity of the virus outside is decreased, the intensity inside will decrease accordingly (10). The hypothesis is based on the principle of Le Chatelier (11).

The principle of Le Chatelier represents self-organization in nature, as it defines the direction in which the system will move to cope with the change of system conditions. When a system in equilibrium is subjected to changes caused by factors such as concentration, temperature, or pressure, the system tends to shift its equilibrium position to counteract the effect of the disturbances without changing the equilibrium constant. Consider a beaker filled with water, at a certain temperature, pressure, and concentration, the liquid water is in equilibrium with the water vapor that forms above the surface of the liquid. The rate of condensation (vapor to liquid) is equal to the rate of evaporation (liquid to vapor); *Figure 1A*. When a stress is applied to the system that allows some of the water vapor to be removed, then, according to Le Chatelier's principle, the rate of evaporation exceeds the rate of condensation (*Figure 1B*) and more liquid water is transformed into vapor until equilibrium is restored (*Figure 1C*), thereby reducing the volume of liquid and water vapor simultaneously (12). For this reason, the evaporation of water is accelerated by

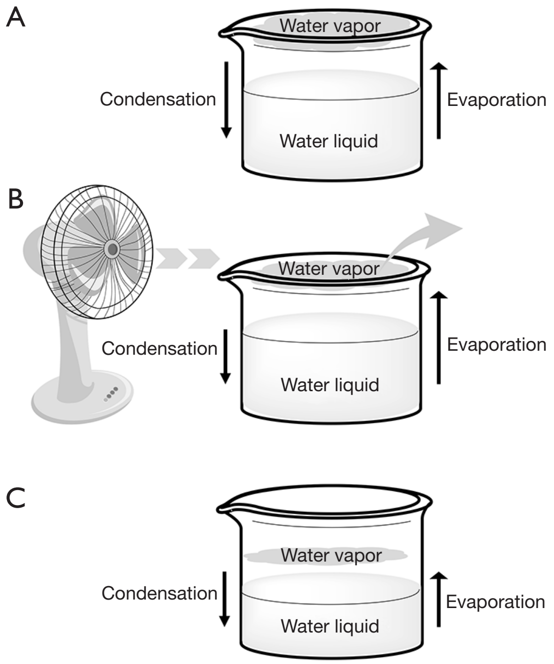

Figure 1 The implementation of the Le Chatelier principle for the evaporation of water. (A) Liquid water and water vapor are in equilibrium, with the condensation and evaporation rates being equal; (B) when water vapor is exposed to a stress, such as an air fan, the vapor is moved away from the surface and the vapor concentration is reduced; at this point the evaporation process is accelerated to counteract the stress; (C) the stress is removed and the equilibrium is restored.

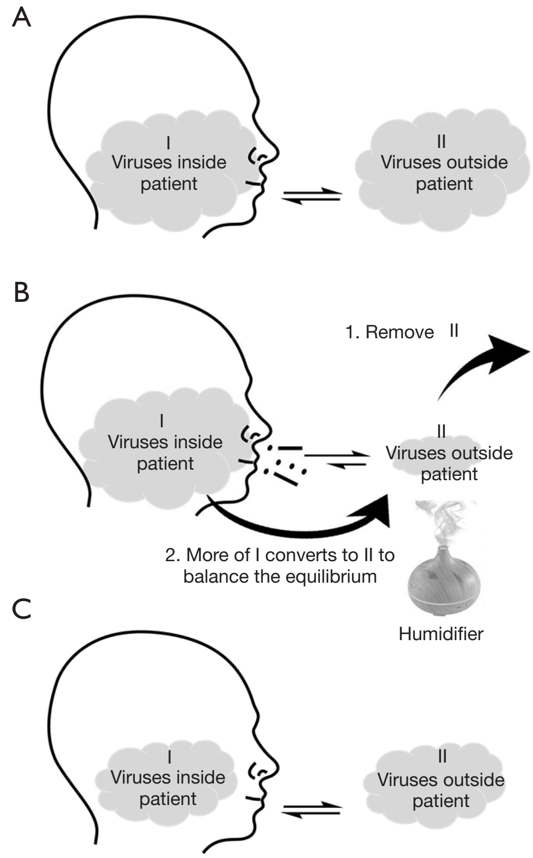

Figure 2 Implementation of Le Chatelier's principle as a potential therapy for the coronavirus. (A) The intensity of the viruses in and outside is in equilibrium; (B) the movement of the viruses from the inside, I, to the outside, II, is increases as a result of external stress (humidifier); (C) enough of I moves to II, so that the equilibrium is restored.

increasing the temperature or reducing the vapor pressure by means of an air fan or rotary evaporator.

Human being is a very important biological system, complex but responsive to different states; strong, weak, happy, angry, young, old, healthy, sick. The intensity of these states is strongly influenced by changes in ion concentration, potential energy, entropy, longevity, and diffusion. These processes exist in the biological system and play an important role in determining the direction and the intensity of the state. The non-biological system tends towards equilibrium, whereas biological system tends towards homeostasis (13). Le Chatelier's principle can be adapted to the biological system and might be used to cope with diseases and maintain a compatible and homeostasis system.

In the case of coronavirus infection, we postulate that the intensity (concentration) of coronaviruses in the patient's body (inside) and in the patient's surroundings (outside) is at a constant ratio (*Figure 2*). Assuming that the intensity of the coronaviruses in the patient's surroundings (outside) would decrease as a result of a stress disorder, it can be predicted according to Le Chatelier's principle that sneezing and coughing would shift the balance from the inside to the outside and thereby reduce the intensity of the coronaviruses in the patient's body. Sneezing, coughing and tears are produced to fight infections and the average number of particles exhaled per cough and sneeze is 5×10^3 and 1×10^6, respectively (14). The movement of the viruses from the inside, to the outside, is continued until equilibrium is restored. The observation is supported by the theory of concentration gradients; substances move from a high concentration area with high potential to a low concentration area with high entropy. This movement is spontaneous and entropy-driven, the result is a concentration gradient, and diffusion continues until this gradient is eliminated. All cells form concentration gradients between their inner and outer fluids by selectively exchanging nutrients, waste products, gases, and ions with their surroundings. Molecules such as water, oxygen, and carbon dioxide use concentration gradients to diffuse freely and transport passively through cell membranes (15).

For the practical implementation of the hypothesis, a specific set is required to increase the entropic state and reduce the virus intensity around the patient. The rational selection of the therapeutic method is crucial to ensure that the virus can be inactivated without harming the patient's health. The most suitable means to reduce the virus intensity around the patient are antiseptics/disinfectants. Antiseptics are used to eliminate microorganisms and/or inactivate viruses on living tissue whereas disinfectants are used on inanimate objects and surfaces. Antiseptics are applied either to the skin or mucous membranes; in the case of pulmonary disease, inhalation therapy can be applied. Most antiseptics/disinfectants have the potential to inactivate viruses, thereby reducing the viral load in the environment. As disinfection progresses, the equilibrium and movement of viruses from the inside of patient's body to the outside continues to shift until the equilibrium is restored. The intensity of the viruses from inside and outside reaches an equilibrium threshold of inactivation, stress is reduced, potential energy is restored, and the immune system is boosted more effectively.

Rationalization of the disinfectant

In practice, disinfection effectively reduces the risk of disease transmission and propagation to an acceptable threshold (16). For more effective implementation of the hypothesis, it is important that the antiseptics/disinfectants pass through the channel that the virus uses to enter, settle, integrate, multiply and return more intensively to the periphery to contaminate the surrounding atmosphere (17). Therefore, the rational selection of the disinfectant, that can be administered by inhalation, is essential to ensure that the virus can be inactivated without harming the patient's health. Most of the present antiseptics/disinfectants are toxic when inhaled and could worsen the situation for the patient. Alcohols are known disinfectants that can inactivate the coronavirus within a short time. Experimental observations show that alcohols increase the area per lipid molecule, reduce bilayer thickness, and thus destabilize membranes (18). Inhaled alcohol may initially be associated with pharmacological effects that increase the risk of addiction (19). It is, therefore, necessary to look for alternative antiseptics/disinfectants that are highly effective and compatible with the patient's body, have a buffering capacity, and can be administered by inhalation.

After a literature search, it was concluded that a mixture of bicarbonate and sodium chloride could be the appropriate disinfectant for this purpose. The sodium chloride-bicarbonate mixture is on the market and used as a nasal humidifying spray for treating dryness inside the nose and for dissolving and softening thick or crusty mucus (20). Bicarbonate is amphiprotic, reacts as an acid to form carbonate, and as a base to form carbonic acid and is therefore considered essential for health and has a unique disinfecting effect with a natural buffering capacity (21). The effectiveness of sodium bicarbonate against certain bacteria and fungi is documented. It is known that sodium bicarbonate (5%) alone or in combination with glutaraldehyde inactivates 99.99% of virally contaminated surfaces in a short contact time (22). Sodium bicarbonate (8.4%) affects the respiratory pathogens by inhalation and effectively inhibits the growth of bacteria, fungi, and *M. tuberculosis bacilli* (23).

Proposed treatment and delivery way of bicarbonate mixture

Based on the above information, the target buffer should contain 5% sodium ions with pH close to 7.4, which is identical to the blood's pH. Sodium chloride and acetic acid is added to adjust the pH of the bicarbonate to match the body pH and form a buffer system with high capacity. The sodium ions are small, diffuse easily into the atmosphere, and are likely to create a region with a high ionic concentration gradient (24). Five percent sodium ion is derived from 2% sodium chloride and 3% of sodium bicarbonate, sodium ions from sodium chloride act as a common ion effect, and according to the Le Chatelier principle, the reverse reaction [*Figure 3*: Eq. 3] accelerates in an attempt to reduce the effect of the added sodium ion. As a result, the equilibrium position shifts to the left, slightly lowering the pH from 8.2 to 8.02 and suppressing the formation of the more basic solution, sodium carbonate, which could be produced from the bicarbonate and carbonate equilibrium.

The proposed treatment consists of a mixture of 3% sodium bicarbonate and 2% sodium chloride (pH =8.02).

$$NaHCO_3 + H_2O \rightleftharpoons Na^+_{(aq)} + HCO^-_{3\,(aq)} \quad (1)$$

$$NaCl + H_2O \longrightarrow Na^+_{(aq)} + Cl^-_{(aq)} \quad (2)$$

$$NaCl + NaHCO_3 + H_2O \rightleftharpoons 2Na^+_{(aq)} + HCO^-_{3\,(aq)} + Cl^-_{(aq)} \quad \text{Common ion effect} \quad (3)$$

$$0.34M\ NaCl + 0.35M\ NaHCO_3 + 0.025M\ CH_3CO_2H + H_2O \underset{[pH=7.4]}{\rightleftharpoons} 2Na^+_{(aq)} + HCO^-_{3\,(aq)} + Cl^-_{(aq)} + CH_3COO^-_{(aq)} + H^+_{(aq)} \quad (4)$$

$$2\%\ NaCl + 3\%\ NaHCO_3 + 0.15\%\ CH_3CO_2H + H_2O \underset{[pH=7.4]}{\rightleftharpoons} 2Na^+_{(aq)} + HCO^-_{3\,(aq)} + Cl^-_{(aq)} + CH_3COO^-_{(aq)} + H^+_{(aq)} \quad (5)$$

Figure 3 Ions distribution of sodium bicarbonate, sodium chloride and acetic acid in water.

To the mixture, 3% vinegar (vinegar contains 5% acetic acid and 3% vinegar is equivalent to 0.025 M acetic acid) and 1% flower extract such as rose water or mint fragrance are added to speed up the movement of ions in a refreshing atmosphere (*Figure 3*). The final mixture has a pH of 7.4 with high buffering capacity. It is interesting to note that bicarbonate-buffer therapy can be administered by inhalation or, if necessary, by spraying into each nostril. Best suited to choose the inhalation method as primary bicarbonate prevention/therapy for COVID-19 coronavirus and other serious viral infectious diseases. The inhalation method can be easily performed at home by inhaling the vapor from an electric humidifier that contains the treatment mixture. The movement of vapor generated by the humidifier disperses the virus particles, increasing their entropic state and reducing their potential for infection and transmission. The humidifier and the mixture can be found in practically every household and is affordable for people, primarily in developing countries (25,26).

Though the mechanisms of virus inactivation by chemicals are poorly understood, initial reactions of viruses with disinfectants lead to breaches of the lipid bilayer. In the case of the sodium chloride-bicarbonate mixture, ionized particles such as Na^+, Cl^-, HCO_3^- saturate the surrounding atmosphere and attract viruses electrostatically via a membrane protein amino acid residue, preferably building blocks with electrically charged side chains. The high ion concentration produces a high osmotic effect, potentially leading to an increase in liquid density, which is associated with water removal from the virus. When the ion concentration is increased, the strength of the electric field accelerates the flow of ions, which in turn increases the collision of the ions with the viruses and eventually leads to an exponential decrease up to a threshold where the virus is inactivated, however, it is unknown how much damage must be done to the viruses before a virus infection can be prevented (27). Since the fusion of the virus with the target cell membrane is enhanced at low pH, the mixture of sodium chloride, bicarbonate and acetic acid is an ideal buffer solution that is compatible with the human body and contributes to maintaining the homeostatic pH.

Conclusions

During the last 20 years, three novel human coronaviruses emerged, and probably more viruses will appear. COVID-19 coronavirus continues to spread and infect more people every day. Even though several available drugs and new vaccine reported to have different degrees of success, still COVID-19 officially has no cure and third wave has already started in certain countries. Viruses have a high mutational propensity that reduces vaccine efficacy, thereby non-specific, non-selective viral inactivation is considered more effective. Antiseptics/disinfectants have the potential to inactivate the virus non-specific non-selective. The proposed method has high potential for preventing and/or treating coronavirus patients and could be effective for the treatment of other viral infections as well. Treatment has no limitations in terms of mutation, availability and cost. It is readily available at most households and is cost-effective for people worldwide to obtain and use. We believe patients infected with COVID-19 should be allowed to apply this treatment and the treatment should be publicly made available to them. The same method can be applied for effective disinfection and prevention of the disease.

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Footnote

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jphe-20-132). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

1. Zhang C, Huang S, Zheng F, et al. Controversial treatments: an updated understanding of the coronavirus disease 2019. J Med Virol 2020;92:1441-8.
2. Walsh EE, Frenck RW Jr, Falsey AR, et al. Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. N Engl J Med 2020;383:2439-50
3. Brufsky A. Hyperglycemia, hydroxychloroquine, and the COVID-19 pandemic. J Med Virol 2020;92:770-5.
4. Gordon CJ, Tchesnokov EP, Woolner E, et al. Remdesivir is a direct-acting antiviral that inhibits RNA-dependent RNA polymerase from severe acute respiratory syndrome coronavirus 2 with high potency. J Biol Chem 2020;295:6785-97.
5. Alzeer J. Halalopathy: a science of trust in medicine. J Integr Med 2019;17:150-4.
6. Norwich KH. Le Chatelier's principle in sensation and perception: fractal-like enfolding at different scales. Front Physiol 2010;1:17.
7. Alzeer J. Entropy and potential energy as a key role of halalopathy in disease prevention and cure. Longhua Chin Med 2020;3:20.
8. Paulo AC, Correia-Neves M, Domingos T, et al. Influenza infectious dose may explain the high mortality of the second and third wave of 1918-1919 influenza pandemic. PLoS One 2010;5:e11655.
9. To KK, Tsang OT, Leung WS, et al. Temporal profiles of viral in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study. Lancet Infect Dis 2020;20:565-74.
10. Burgess S, Smith D, Kenyon JC, et al. Lightening the viral load to lessen covid-19 severity. BMJ 2020;371:m4763.
11. Quílez-Pardo J, Solaz-Portolés JJ. Students' and teachers' misapplication of Le Chatelier's principle: implications for the teaching of chemical equilibrium. J Res Sci Teach 1995;32:939-57.
12. Debenedetti PG. editor. Metastable liquids: concepts and principles. Princeton: Princeton University Press, 1996.
13. Kotas ME, Medzhitov R. Homeostasis, inflammation, and disease susceptibility. Cell 2015;160:816-27.
14. Nicas M, Nazaroff WW, Hubbard A. Toward understanding the risk of secondary airborne infection: emission of respirable pathogens. J Occup Environ Hyg 2005;2:143-54.
15. Zielińska-Dawidziak M, Grajek K, Olejnik A, et al. Transport of high concentration of thiamin, riboflavin and pyridoxine across intestinal epithelial cells Caco-2. J Nutr Sci Vitaminol (Tokyo) 2008;54:423-9.
16. Sato J, Miki M, Kubota H, et al. Effects of disinfectants against norovirus virus-like particles predict norovirus inactivation. Microbiol Immunol 2016;60:609-16.
17. Hong JK, Lee KN, You SH, et al. Inactivation of foot-and-mouth disease virus by citric acid and sodium carbonate with deicers. Appl Environ Microbiol 2015;81:7610-4.
18. Eslami H, Das S, Zhou T, et al. How alcoholic disinfectants affect coronavirus model membranes: membrane fluidity, permeability, and disintegration. J Phys Chem B 2020;124:10374-85.
19. MacLean RR, Valentine GW, Jatlow PI, et al. Inhalation of alcohol vapor: measurement and implications. Alcohol Clin Exp Res 2017;41:238-50.
20. Burgess WP, Walker PJ. Mechanisms of contrast-induced nephropathy reduction for saline (NaCl) and sodium bicarbonate (NaHCO3). Biomed Res Int 2014;2014:510385.
21. Mitaka T, Sattler GL, Pitot HC. The bicarbonate ion is essential for efficient DNA synthesis by primary cultured rat hepatocytes. In Vitro Cell Dev Biol 1991;27A:549-56.
22. Malik YS, Goyal SM. Virucidal efficacy of sodium bicarbonate on a food contact surface against feline calicivirus, a norovirus surrogate. Int J Food Microbiol 2006;109:160-3.

23. El Badrawy MK, Elela MA. Yousef AM, et al. Effect of sodium bicarbonate 8.4% on respiratory tract pathogens. Chest Lung Res 2018;1:3-7.
24. Kanaparthi S, Supraja P, Singh SG. Smart, portable, and noninvasive diagnostic biosensors for healthcare. In: Inauddin, Mohammad A, Khan R, et al. editors. Advanced biosensors for health care applications. Amsterdam: Elsevier, 2019:209-26.
25. Mir MA, Mansoor S, Bhat A, et al. Lysosomotropic properties of sodium bicarbonate and covid-19. Farmacia 2020;68:771-8.
26. Daly JL, Simonetti B, Klein K, et al. Neuropilin-1 is a host factor for SARS-CoV-2 infection. Science 2020;370:861-5.
27. Springthorpe VS, Sattar SA. Chemical disinfection of virus-contaminated surfaces. Crit Rev Environ Control 1990;20:169-229.

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