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Review Article

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Examining Covid 19 from a Novel Perspective

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Abstract

Recently, it was shown that hydroxychloroquine (HCQ) had a positive effect in COVID 19 infection, and this was augmented by the addition of azithromycin (Z). A proposed mechanism of action was outlined as to how these repurposed medications caused this. This short review offers an alternative hypothesis as to how this occurs, namely that the virus creates biofilms that activate the immune system which causes tissue damage. This is similar to other diseases, e.g. psoriasis, in which microbes create biofilms that interact with the immune system, and that interaction leads to the disease. Many other examples of other microbes that do this have been presented. How and where these two medications (HCQ and Z) fit into this hypothetical pathway is discussed. Other repurposed medications known to impact COVID 19 are briefly discussed.

Keywords: Azithromycin; Biofilms; COVID 19 infection; Immune system

Review

Very recently, it has been shown that hydroxychloroquine (HCQ) with (or without) azithromycin (Z) had an ameliorative effect in patients with COVID 19 infection [1]. Previously, both drugs have demonstrated antiviral effects even though one (HCQ) is an antimalarial as well as an anti-inflammatory agent and the other (Z) is an antibiotic. (HCQ) has definite antiviral capabilities with an EC50 of 0.72 while (Z) has unknown antiviral effects[1]. This is the reason these two compounds were selected for this open label, non-randomized trial.

The (HCQ) administered separately showed a significant (p=0.001) viral clearance rate of 70% vs controls. The (HCQ), with the addition of (Z), presumably for the worst clinical cases, was given to 2 patients with upper respiratory tract disease and 4 patients with lower respiratory tract disease. Each in the latter group had pneumonia on CT scanning. The combination (HCQ + Z) yielded 100% clearance of the virus [1].

This is an important study for it showed that repurposing two medications may be useful in combatting this viral pandemic. The limitations, mostly alluded to by the authors, were lack of inclusion of the "intent to treat" patients, three of whom were transferred to ICU and one who died. Other limitations included lack of important clinical details, such as did the fevers abate when viral clearance (from the nose) was demonstrated? Similar clinical data as to the state of the pneumonia after viral clearance was lacking.

An alternative hypothesis may have some credibility, namely that this virus may create biofilms that, in turn, lead to many changes including cytokine production and tissue destruction. This pathway would be in keeping with many other diseases caused by microbes that create biofilms that create disease.

In nature, more than 90% of microbes live in biofilms and, with pathologic microbes, many disparate diseases seem to be generated by this process [2,3]. These include cutaneous diseases such as atopic dermatitis, psoriasis, leprosy, and many others [4-6]. Internal diseases include arthritis, otitis media, arteriosclerosis, cystic fibrosis, and Alzheimer's disease and others[7-11]. Somewhat surprisingly, biofilms have recently been found in gouty tophi and rheumatoid nodules [12,13].

To date, viral diseases associated with biofilms include HTLV1, molluscum contagiosum, and human papilloma virus (in squamous cell carcinoma in situ in organ transplant patients of color) [14-16]. The viral biofilms were found intracellularly because the microbe had to "hi-jack" the cell's DNA to replicate

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and form the necessary quorum of organisms to create the biofilm [14]. The development of viral biofilms, as noted, may lead to significant clinical changes. This may allow other (secondary) pathogens that also make biofilms, such as staphylococci, to proliferate. These other organisms may also incorporate the virus and other organisms into the biofilm matrix. This concept has been elegantly demonstrated with Borrelial biofilms incorporating Chlamydia pneumoniae in the center of the biofilm [17].

Of interest, both (HCQ) and (Z) have biofilm dispersion capabilities [18]. The (HCQ), as an antiviral and a biofilm disperser would seem the ultimate antiviral weapon. Interestingly, the addition of (Z) to the protocol added increased efficacy. (Z) has antiviral effects, but the mechanism for this is not understood. Its antibiofilm capabilities are somewhat better characterized.

Other repurposed medicines such as remdesavir (R) and sarilumab (S) have also been shown to have a positive impact on COVID 19 [19,20]. R is an antiviral, so it is active at the beginning of the hypothetical cascade. S is an Interleukin 6 inhibitor that is active near the end of that cascade(**Figure 1**).

Pathway from virus to tissue destruction



Figure 1:Cascade showing where different agents likely act.

The situation in the more severe COVID 19 patients needs much more microbiological and pathological scrutiny. For instance, is the periodic acid Schiff positive colloid found in the lungs (alveoli) of acute respiratory distress syndrome actually a biofilm? And, is it created by a different organism, such as staphylococcus, because it is entirely extracellular? It should be possible to bring more understanding to this disease relatively easily.

References

- https://drive.google.com/file/d/186Bel9RqfsmEx55FDum4xY_IIW-SHnGbj/view accessed 3/18/20
- Tasneem U, Yasin N, Qasim M, Nisa I, Rasheed U, et al. (2018) Biofilm producing bacteria: A serious threat to public healthindeveloping countries. J Food SciNutr 1: 25-31.
- Allen HB, Cusack CA, Joshi SG (2019) The Impact of Biofilms in Alzheimer's disease compared to Other Diseases in Which They Play a Role. Int J Neurobiol 1: 115.
- Allen HB, Vaze ND, Choi C, Hailu T, Tulbert BH, et al. (2014) The presence and impact of biofilm-producing staphylococci in atopic dermatitis. JAMA Dermatol150: 260-265.

- Allen HB, Jadeja S, Allawh RM, Goyal K (2018) Psoriasis, chronic tonsillitis, and biofilms: Tonsillarpathologic findings supporting a microbial hypothesis. ENT J 97: 79-82.
- Allen HB and Moschella SL (2017) The Role of Rifampin in Leprosy: Leprosy Through a New Lens. JAMADermatol Published online 153: 261-262.
- Jacovides CL, Kreft R, Adeli B, Hozack B, Ehrlich GD, et al. (2012) Successful identification of pathogens by polymerase chain reaction (PCR)-based electron spray ionization time-of-flight mass spectrometry (ESI-TOF-MS) in culture-negative periprosthetic joint infection. J Bone Joint Surg Am 94: 2247-2254.
- Bakaletz LO (2007) Bacterial Biofilms in Otitis Media: Evidence and Relevance. Pediatr Infect Dis J 26: S17-9.
- Allen HB, Boles J, Morales D, Ballal S, Joshi SG (2016) Arteriosclerosis: The Novel Finding of Biofilmsand Innate Immune System Activity within the Plaques. J Med SurgPathol 1: 135.
- Moreau-Marquis S, Stanton BA, O'Toole GA (2008) Pseudomonas aeruginosa biofilm formation in thecystic fibrosis airway. PulmPharmacolTher 21:595-599.

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- Allen HB, Allawh RM, Goyal K (2018) A pathway to Alzheimer's disease. J CurrNeurobiol 9: 29-32.
- 12. Allen HB, Cusack CA, Allen RA (2019) The Presence of Biofilms in Gouty Tophi. Clinical Microbiologyand Research 1: 2-2.
- Allen HB. Yi Z, Roberts AA, Allen RA (2019) Biofilms in Rheumatoid Arthritis Nodules: A Novel ClueRelating to Microbial Origin. Microbiol Infect Dis 3: 1-2.
- Pais-Correia AM, Sachse M, Guadagnini S, Robbiati V, Lasserre R (2010) Biofilm-like extracellular viral assemblies mediate HTLV-1 cellto-cell transmission at virological synapses. NatMed 16: 83-90.
- Allen HB, Allawh RM, Ballal S (2017) Virally-Induced, Intracellular Biofilms; Novel Findings inMolluscumContagiosum. ClinMicrobiol 6: 302.

- Allen HB, Chung CL, Allawh RM, Larijani M, Cusack CA (2019) Biofilms in Squamous Cell Carcinomaln Situ. ClinDermatol Dermatitis 2:110.
- Sapi E, Gupta K, Wawrzeniak K, Gaur G, Torres J, et al. (2019) Borrelia and Chlamydia Can Form Mixed Biofilms inInfected Human Skin Tissues. Eur J MicrobiolImmunol9: 46-55.
- Wang A, Wang Q, Kudinha T, Xiao S, Zhuo C (2016) Effects of Fluoroquinolones and Azithromycin onBiofilm Formation of Stenotrophomonasmaltophilia. Sci Rep13:29701.
- 19. https://www.statnews.com/2020/03/16/remdesivir-surges-aheadagainst-coronavirus/
- 20. https://www.pmlive.com/pharma_news/sanofi,_regeneron_launch_trials_of_arthritis_drug_kevzara_for_covid-19_1329326

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