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Four Entities, Three Theories and Four Scenarios Under the Umbrella of the Second Infection for the SARS-COV-2- Virus in Man

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Abstract
The four entities that were overlapped in the sense with post recovery second sars-cov-2 infection in man were as; Re-infection ,co-infection, reactivation infection and stealth infections Three theories tempts to explain the case. Together with a trial to delineate in between them. The infection course may be ;Asymptomatic ,mild, and moderate and severe. The tissue tropism of the virus is lung, then to renal and nervous tissues. The virus genome variate in to six molecular genetic clades, two biotypes as Asian and European, and six patho-types. The co-infectents are: Herps ,adeno ,measles viruses ,S. aureus, N. cattrahalis and Klebsiella. The virus immune-dominant epitopes can induce effector B, memory B, effector auto-reacting B, memory auto-reacting T , effector T and memory T and mucosal invariant T cells. The resulting immune responses are humeral, cellular ,mucosal invariant T cell responses in addition to autoantibody responses. The net results of these responses may terminated by by production of specific antibodies and cytokine and may accompanied by humeral and /or cellular enhancement of the disease. The apparent duration of post-infection immunity seems to be short and the protection efficacy still a matter of debate and four post-recovery immunity scenarios were suggested as sterilizing ,functional ,waning ,and lost immunities.
Keywords: Co-Infection ,infection, re-infection ,reactivation infection ,scenarios.
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1. Introduction
When a case of post-recovery from sars-cov-2 infection contracts another infection, the definition of the case may overlap in between more than one concept. Under the ambrella of the other infection ,four, entities may share some of their characteristic aspects(Dictionary .Com, Gaafaas 2018,Marti 2001,Kumar et al.2018).The objective of the present opinion was to delineate such overlapping aspects through exploring the available standard definitions(Dictionary.Com ,Gaafaas 2018,Martin 2001,Kumar et al.2018,Yoa et al.2014) per each entity with their foreseen evidences and examples.

2. Source
The source of the infection constitute the normal growth habitat of the virus in the animal reservoirs and environmental utensils(Cruickshank et al.1973).

3. Transmission
The human cough and the sneeze flying droplets and becoming air born ,close contact with the patients or with the house hold infected animals, contact with the animal reservoirs[Bats, Pengalon] , and raw animal derived food consumption. Close contact with human sputa, urine, feces and blood of the patients.(Chan et al.1013).

4. The virus
The morphology of the virus Sars-cov-2 are being round, elliptical or even of pleomorphic morpho-types with spherical symmetry. They are single positive strand RNA viruses with crown like appearance due to the glycoprotein spikes on the envelope surface .The virus is sensitive to heat[to certain limits] ,UV, ethanol 75% and chlorine containing antiseptics(Chen et al.2020).

5. Infection
The invasion of the body by the pathogenic virus capable of causing disease. The reaction of the tissues in their presence and the toxin produced by them(Combs 1976).The condition in which pathogenic virus have become established in the tissue of the host. Though such establishment does not eligibly constitute or lead to disease. The term infection is often used parallels to disease(Singleton & Sainsbury 1980).The infection as a term has more than one meaning.one meaning ,however, is to describe infectious disease. The infection mechanism can be made through ; i-Production of virulence factors and ,ii-Invasion and inflammation(Levinson et al.2018).Virus infection effect on the host cell may took four main types; i-Death , ii-cell fusion , iii-malignant transformation , iv-no apparent effect. On whole human being level , however ,it will be as ; i-transmission and entry to the cell ,ii-

replication of the virus and damage ,iii-spread to other cells ,iv-immune responses as a host defense mechanisms and as contributing cause of disease , ,v-Persistence in some instances(Levinson et al.2018).The details of the infection mechanisms are depicted in Table 1.

Table 1:Sars-Cov-2 infection mechanisms[Chan et.al,2019]

i-Port of entry: Eye ,nose ,mouth
ii-Gain foothold: Primary site lung cells. Secondary sites ,enterocyte ,renal and nerve cells
iii-Cell entry: Through ACE2 in lung ,gut, kidney and nerve cells
iv-Replication: viron particles production, cytopathic effect, cell lysis and release.
v-Virus immune cell interaction: NK cell kill the virus infected cells, macrophage pino-cytose the free virus present its antigenic peptides to helper T cells, immune recognition .Effector and memory cell production
vi-Immune responses: Neutralizing antibodies ,activated CD4,CD8 T cells ,cytokine production .Autoantibody and auto-reacting B and T cell production
vii-Immune tissue injuries: Cytokine storm, ,micro-thrombi ,humoral and cellular disease enhancements viii-Four post-recovery immunity scenarios were suggested .

6. Re-infection;

There are several definitions for the term re-infection .The first is a secondary infection ,or the infection that follows an infection by different type or different strain(Dictionary .Com) .The second as Reinfection can be defined as a second infection that follows recovery from previous infection by the same causative agent(Haseltin 2020). The third is as the reappearance of the virus infection at least after one to four months of the demonstration of that infection which is caused by different virus[Gaafaas 2018].The fourth however ,is an infection following recovery from or superimposed on infection of the same type(Mariam Webster Dictionary).Finally the fifth is as a second infection that follows a previous infection by the same causative agent(Your Dictionary Home Page).Several reported cases for covid -19 reinfection were published during this pandemic. The criteria for re-infection delineation[Kotecha & Bird 2020) are;

i-An initial sars-cov-2PCR confirmed acute covi-19 disease.

ii-Clinical recovery, discharge with at least one Sars-cov-2 negative PCR test

iii-Followed by confirmed Sars-cov-2 positive PCR test at least 28 days after the previous Sars-cov-2 negative PCR test.

7. Stealth Infections;

There were two views concerning the stealth viruses. The first imply stealth spread of the sars-cov-2 virus in the community(Advisory Board Research Daily Briefing 2020).While the second concerned with the stealth adapted virus, in which part of the capsid proteins are lost and the virus in such a case pass unrecognized by the cellular immune system of the proteins .When the stealth adapted viruses retain the ability to damage cells they can potentially cause persistent infection leading to prolonged illness. The viral nature of such illness is usually overlooked due to absence of overt inflammation. The term stealth was denoted to a basic property of evading effective immune recognition(Martin 2001).So far search in the to date literature indicated that there is no evident differentiation criteria for discrimination from the other entities(Martin 2001,Advisory Board research Daily Briefing 2020).

8. Co- Infections;

It is the simultaneous infection of a cell or organism by separate viruses. It is used interchangeably to super-infection and/ or mixed infections. The meaning depends on the context whether applied for a single cell, cell line or part of the host or whole of the host. Co-infection may lead the genetic exchange between the two infecting viruses to the same cell generate recombinant viruses. Co-infection in general may have a role in reducing or augmenting disease severity (Kumar et al.2018). Viral-viral co-infections do not add to severity of the disease with single infections and might be in some cases be protective of the severe diseases(Meskill & O Berin 2020).The risk of testing positive for sars-cov-2 was 68% lower among infected positive cases suggesting competition between the two viruses. Such competition may be due to immune mediated interference resulting to diminishing of the first virus during the peak of the other virus .Co-circulation of influenza and sars-cov-2 could have a significant impact as morbidity, mortality, and health service demands(Stowe et al. 2020).Sars-cov-2 may co-infect with a number of other virus groups as in the case of measles, adeno, and herpes viruses. The co-infecting non-sars-cov-2 viruses rates were significantly higher than 86% in sarsco-2 positive than in sars-cov-2 negative. Ageing ,nursing home status associated with higher sars-cov-2 infection and co-infection rates(Massey et al.2020).The suggested(Kumar et al.2018,Meskill & Oberin 2020,Stowe et al.2020, Massey et al.2020) criteria for differential discrimination are;

i-An initial simultaneous Sars-cov-2 and other virus identified in same sample or on other replicate of the same sample

ii-An initial clinical recovery for reasonable short time in a couple of days.
iii-followed by the initiation of other symptoms indicating emergence of other infection
The reported co-infecting microbes are; measles ,herpes virus, adenovirus, N. catarrhalis ,Klebsiella and S. aureus(Massey et al.2020).

9. Reactivation Infections;

Reactivation Infections: The process of viral replication is of complicated nature.it involves different steps from the time a virus binds to the target cell until the release of new progeny virons outside of the infected cell. An active replication of the viral genomes lead to lytic infection characterized by the release of new progeny. Though upon the lysis of the infected cell, another mode of viral infection is the latent infection phase where the virus is quiescent[a case in which the virus is not replicating]. The active and latent infection are combined, where the virus replication involves stages of both silent and productive infection without rapidly killing or even producing excessive damage to the host cells. Virus reactivation is the process by which a latent virus switch to the lytic phase of replication. To initiate virus reactivation in-vivo ,a combination of both external and/or internal cellular stimuli are needed(Traylen et al.2011).The latent virus infection upon reactivation can cause recurrent infection .Both of the primary and recurrent infections can induce disease like the case of experimental murine HSV-1 encephalitis(Yao et al.2014).Some workers holds the idea of post-recovery second infection or switching of the latent to active replication do happened in covid-19(Cummins 2020).The reactivation of a previously negative test results reached the percentage of 5 out of 55 patients(Ye et al.2020,Ro 2020).The possible suggested criteria (Yao et al.2014,Traylen et al.2011,Cummins 2020,Ye et al.2020,Ro 2020)for determination of reactivation are;
i-An initial Sars-cov-2 PCR positive Clinical sample of the patient
ii-Clinical recovery with at least one Sars cov-2 negative sample
iii-Followed by confirmed positive Sars-cov-2 PCR test but with rather different genomic structure from latent dormant intracellular infection. Till now no sure reported Covid -19 reactivation case reported might be due to difficulty in detection of cellular dormant virus from human being in the affected nervous tissues ,Table 2.

Table 2 :The second infection four entities. A comparative view.

Features	Re-infection	Co-infection	Reactivation infection	Stealth infection
Virus source	Two successive virus infection from outside	Two simultaneous virus in the same time from outside the cell	The first exogenous and the second latent reactivated on drop of immunity	-exogenous stealth spread -latent capsid antigen and tissue hidden on drop of immunity reactivated
Timing of the onset	Post-recovery	Simultaneous	Post-recovery	-First infection -Hidden reactivate post-recovery
Infection course	Second to the other mild or sever	Infection processes done on same time	Secondary post to recovery time may be mild to sever	-mild to severe

10. Laboratory Biology;

Nasal and throat swabs were taken from the suspect preserved in a transport media for rural areas samples. For the civilians sample taken in laboratory. These samples will be processed for cell isolation ,then for cellular genome isolations. The isolated RNA amplified through RNA Q time PCR to watch the presence of Sars-cov-2 virus genome .Paired blood sample one at the time of the onset and the other on the or post to recovery for detection of specific Ig M ,IgA and IgG .C reactive protein will be of help to delineate the infection/inflammation course, Table 3,(European Centre for Disease Prevention and Control, ECDPC .2020). Table 3:Laboratory biology Investigations for Sar-cov-2 infections(ECDPC2020)

Table 3. Laboratory biology Investigations for Sar-cov-2 infections(ECDPC2020)

Nucleic acid test/ A-results B Duration C-Viability D-Test Frequency	Real positive False positive for 104 days post to onset of the infection Persistent positive may not indicate viability .It may be nonviable. Need to validated At the onset one, post-recovery two sequential test	Real negative False negative Intermittent negative
Sero-conversion	Paired sera one on the onset and the other at recovery	
Ig class determination	At 7-10 days post the onset and one after three weeks of the onset	

11. Theories

The nature of sars-cov-2 disease as evident from the to date literature. There was an emergent suggestion of three theories giving an explanation to the post-recovery second infection as ;re-infection, reactivation and false negative(Varshneg 2020)..

12. Scenarios

Four scenarios were suggested for the covid-19 post-recovery immunity as; sterilizing ,functional ,waning and lost immunities(Branswell 2020).

13. Concluding Remarks

virus was mapped for biotype, and genotype .Two biotypes and six molecular genetic clads .Reservoirs hosts were pangalon, the ant eater and bats .Infection cycles are anthropophilic and zoo-anthropophilic. Three theories for explanation of the post-recovery second infection are known as ; re-infection ,reactivation infection and false negative results in PCR. Infected hosts are of low, medium and high immune responses. Immune responses are of; Antibody humoral ,T cell ,mucosal invariant T cell and autoantibody responses. Immune tissue injuries of the infected hosts can be; cytokine storm ,micro-thrombi, humoral immune and cellular immune enhancement of the disease. Post-infection immunity seems to be short. The post-recovery immunity were suggested as ;Sterilizing, functional, waning and lost.

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